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BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 2 1941

THE TOXICITY OF SULPHONAMIDE DRUGS TO CELLS IN VITRO*

BY

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(WITH SPECIAL PLATE)

The administration of sulphonamide drugs by injection or by mouth for the prevention and treatment of wound infection is in many cases giving place to a more direct method, in which the powdered drugs are applied locally to the wound surfaces (Jensen, Johnsrud, and Nelson, 1939; Legroux, 1940; Colebrook, 1940; Hawking and Piercy, 1941; Colebrook and Francis, 1941; and others). The first method yields concentrations in the blood and tissue fluids usually ranging from 1:10,000 to 1:100,000, while the second establishes local concentrations ranging from saturation strength downwards. This second method raises problems concerning the toxicity of sulphonamide drugs to living cells which could hardly be expected to arise in acute form after other methods of treatment. Tissue culture provides one method of studying problems of this sort, because it is capable to some extent of reproducing *in vitro* the influence of the drugs on the behaviour of the various types of cells which play a part in wound healing. By means of it one should be able not only to rank a series of drugs in the order of their toxicity to living cells, but also to obtain a clear idea of the order of magnitude of the concentrations which are lethal to them.

The drugs chosen for investigation were sulphanilamide, sulphathiazole, sulphapyridine, and (in some tests) sulphadiazine; and various aspects of their influence on the behaviour *in vitro* of cells of three main types—fibroblasts, macrophages, and epithelia—have been put on record. In each case it has been possible to draw an instructive comparison between the action of the sulphonamide drugs and that of proflavine.

The method of direct application has been kept constantly in mind. For instance, a comparison of the drugs at equal or chemically equivalent concentrations alone would be misleading, for their *effective* toxicity depends largely upon solubility, and on other factors—such as the rate of transport from a site of local application—which themselves largely depend upon solubility. The basic cultivation media—adult chicken plasma or serum, in some cases with the addition of chick embryonic extract—are those which have come to be regarded as standard in cultivation work. None of the sulphonamide drugs affects the coagulation of plasma, and none is notably surface-active. Except with the highest concentrations of sulphanilamide, where a slight but significant osmotic effect must be exerted, the interpretation of experimental results is not therefore complicated by secondary reactions of the reagents employed. Sulphonamide drugs prove, however, to be considerably more soluble in serum than in Tyrode's solution (see table, p. 153).

I. Action of Sulphonamide Drugs on Fibroblasts of a Cultivated Strain

Willmer (1933) and Willmer and Jacoby (1936) have described a technique for recording mitotic activity and cell-movement rate in fibroblast colonies which has given consistent results for some years under a wide variety of conditions. In principle it consists in photographing directly on 3-inch bromide paper film a sample of cells (100 to 400) from the peripheral part of a colony of fibroblasts growing in Carrel flasks to which a photographic glass base has been fitted. The photographs are taken automatically at six-minute intervals through specially designed inverted microscopes. Estimates of the percentage of cells in the photographic field undergoing mitosis per hour are made by a later detailed analysis of the films.

In the experiments to be described in this section single cultures from a strain of fibroblasts from the frontal bone of a 12-day-old chick embryo were planted into 30-mm. Carrel flasks containing a *coagulated phase*—in which the cells grow—of 0.2 ml. of an equal mixture of plasma and 20% embryo juice in Tyrode's solution, and a *supernatant fluid* of 1 ml. 20% embryo juice in Tyrode. "100% embryo juice" is the undiluted fluid removed by centrifugation from 8-day-old chick embryos crushed in a Latapie press. After twenty-four hours' cultivation at 38° C. a sufficient number of cells wander into the medium to make photography possible. Normal growth is recorded for approximately four hours. The supernatant fluid is then replaced by 1 ml. of a solution of the appropriate drug in a medium otherwise identical. The response of the cells to the drug is recorded for fourteen to eighteen hours, after which the supernatant fluid is again replaced by 1 ml. of 20% embryo juice in Tyrode. In short, it is possible over a stretch of twenty-seven to thirty hours to record normal growth, the action of the drug, and the nature of the recovery of the cells, if any takes place, from the action of the drug.‡

In analysing the results the hourly fluctuation in mitotic rate is smoothed out by calculating the mean mitotic

* A report to the War Wounds Committee of the Medical Research Council.

† For the expenses of the research this author is indebted to the Research Committee of the University of Birmingham and to the Medical Research Council.

‡ For the maintenance of these cultures and other technical assistance, one of us (E. N. W.) is indebted to Mrs. Simon Reuss.

percentage over three-hour stretches, an adjustment which does not obscure major trends in the curve of growth. By this method the actions of sulphanilamide, sulphathiazole, and sulphapyridine have been tested at final concentrations in the culture flask corresponding to about 70% of that at which the drugs are saturated in Tyrode's solution at 38° C.* The results of these experiments, and others in which the drugs were applied at lower concentrations, are illustrated in Chart I (i, ii, iii). They may be summarized as follows:

Sulphanilamide at a final concentration of approximately 1:100 in the culture flask brings the division and migration of the cells to a standstill. Both are resumed within five hours after removal of the drug from a treatment lasting fourteen to eighteen hours (Chart I, iii, *b*). At a concentration of 1:1,000 sulphanilamide exerts no depressant action (Chart I, iii, *a*).

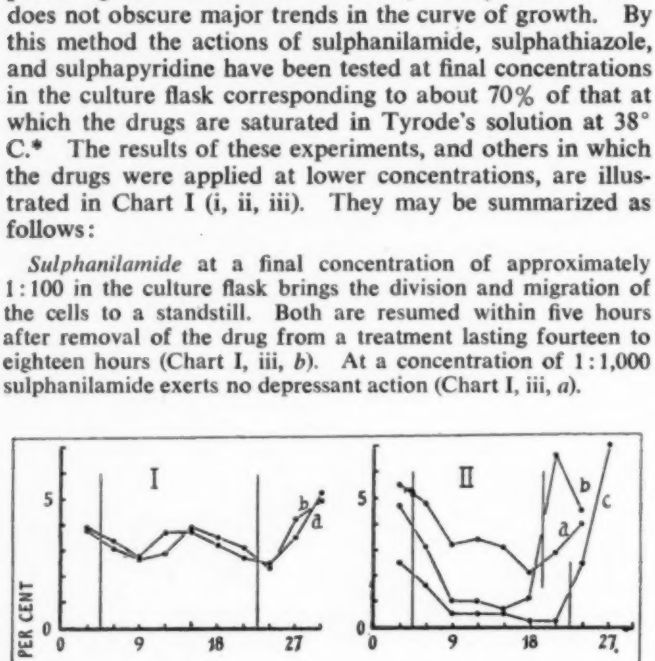

CHART I.—The action of sulphonamide drugs and proflavine on fibroblasts of a cultivated strain: the percentage of cells undergoing mitosis per hour, averaged over 3-hour periods (vertical axis), as a function of the time of incubation (horizontal axis). The vertical lines enclose the stretch over which the drugs were applied in solution in 20% embryo juice in Tyrode. The final concentration in the culture flasks corresponds to about 70% of the figures quoted. (i) *a*, *b*, Sulphapyridine 1:1,000. (ii) *a*, Sulphathiazole 1:10,000; *b*, 1:1,000; *c*, 7:700 approx. (iii) *a*, Sulphanilamide 1:1,000; *b*, more than 1:100. (iv) Proflavine 1:1,000,000.

Sulphathiazole differs from sulphanilamide in the wide range of concentration (1:10,000 upwards) over which it exerts an appreciable inhibitory effect; but even the 70% saturated solution fails to abolish mitosis completely (Chart I, ii, *a*, *b*, *c*). Recovery from fourteen to eighteen hours' subjection is rapid and complete, and shows a marked tendency towards compensatory overgrowth.

Sulphapyridine fails to affect mitosis or migration in 70% saturated solution (Chart I, i, *a*, *b*).

The order of increasing *effective* toxicity is therefore simply that of increasing solubility, although sulphathiazole appears to be the least favourable for growth at any assigned concentration. Only sulphanilamide could be expected to exert a clinically significant inhibitory action, but particular attention should be paid to the fact that recovery from its action under the conditions described here is rapid and complete. In marked contrast to these results are those from proflavine (Chart I, iv), which exerts a *total* and *irreversible* inhibitory effect, accompanied by disintegration of cells, at concentrations lower than 1:1,000,000.

* The solutions referred to in this section as "saturated" were prepared by prolonged incubation of an excess of the crystals in Tyrode (*p*H 7.8) at 38° C., followed by immediate Seitz filtration. The concentrations were found to be: sulphapyridine, 1:1,000 approx.; sulphathiazole, 1:700 approx.; sulphanilamide, *more than* 1:100.

II. Action of Sulphonamide Drugs on Freshly Explanted Fibroblasts

The preceding section records the action of sulphonamide drugs on tissues which have been grown for upwards of four passages (8 to 12 days) *in vitro*. It can be shown that during the course of cultivation the power of tissue fragments to resist the action of inhibitory substances rises sharply to a figure which eventually becomes constant and which is characteristic only of a particular "strain" of cells. Tests of an alternative type to those described in Section I can be devised which take advantage of the fact that *freshly explanted* tissues of a given source and embryonic age possess a characteristic power of resistance to growth inhibition. These tests consist in determining the concentration of a drug which is sufficient and necessary to suppress all outgrowth from a standard explant for 24 hours at 37° C. The method has been described by Medawar (1937, 1940). The standard explant is a fragment of the wall of the ventricle of a 10-day-old chick embryo heart, and the standard medium consists of 0.1 ml. of an equal mixture of cockerel plasma and a solution of the drug in Ringer's solution. Falling dilutions of the drug are prepared, at each level of which five or ten explants are incubated in separate cultivation chambers. After twenty-four hours it is easy to determine by inspection the concentration which is just high enough to inhibit all outgrowth. In the neighbourhood of this "threshold point" concentrations of the drug differing from each other by less than 10% are distinguishable.

After 48 hours' subjection to the action of the drug a further test can conveniently be applied. This consists in reculturing each explant, after washing for one hour in Ringer at room temperature, into a plasma and embryo-extract medium. A later inspection of these subcultures then provides one type of estimate of the minimum lethal concentration of the reagent used, since it is possible to record what concentration of the drug, under the conditions described, the cultures can withstand for forty-eight hours without being "killed"—i.e., without undergoing changes irreversible by further cultivation in a normal medium. If the drug is comparatively non-toxic the cells are not killed by a concentration *higher* than that necessary to inhibit growth totally; a more toxic substance (e.g., proflavine) will, however, kill the cells at a concentration *lower* than that which allows a certain amount of growth to take place within the first twenty-four hours after explantation.

Results of test of these two types on four sulphonamide drugs may be summarized as follows:

Sulphanilamide.—The threshold point corresponds to just above half the concentration at which the drug is saturated in Ringer at 37° C. (1:150 approx.). Isolated cells which migrate from the explant at this concentration are smaller than normal and highly refringent. Recovery from forty-eight hours' subjection to this concentration is rapid and complete, but fresh explants are not able to withstand twenty-four hours' exposure at 37° C. to a saturated solution of the drug in the culture medium (1:60 approx.†). Osmotic effects as such probably play very little part in these reactions. Heart fibroblasts are capable of withstanding much higher osmotic pressures (e.g., that generated by 5% maltose) for much longer periods.

Sulphathiazole.—The threshold concentration proves to be approximately that at which the drug is saturated in the culture medium at 37° C. in the presence of excess crystals (1:500†). Recovery from forty-eight hours' subjection is rapid and complete. At concentrations as low as one-third of saturation strength cells which migrate into the culture medium during the

† These figures for solubility in 50% plasma are approximations based on the table of solubility in 40% serum which appears later (p. 152).

first day show no further progress between the twenty-fourth and the forty-eighth hour of cultivation.

Sulphapyridine (Plate, Fig. 7) and *sulphadiazine* permit the free migration of fibroblast cells among crystals lying in saturated solution in the culture medium at 37° C., and no reading can therefore be obtained by the method of thresholds. Cells at this concentration show minor abnormalities of a non-specific type—e.g., a tendency towards vacuolization—but are not abnormally refringent. Growth proceeds normally on recultivation. Sulphadiazine is slightly but not in a practical sense significantly more toxic than sulphapyridine.

These results on freshly explanted fibroblasts reinforce those of the previous section. They further suggest that neither sulphapyridine nor sulphadiazine when applied to wound surfaces need be expected to exert any depressant action on regenerative growth.

Proflavine in neutral solution in Ringer reaches threshold strength at a concentration of 1:120,000 (± 5%), but recovery from forty-eight hours' subjection is only possible from an ill-defined concentration in the neighbourhood of 1:250,000. While they indicate that proflavine is a highly toxic substance, these figures are notably lower than those quoted in Sections I and III. The reason for this is probably that proflavine is powerfully adsorbed upon tissues—as it is, for instance, upon glass; so that the *dose* administered is as important as the concentration. The dose applied in the experiments described in Sections I and III is 1γ, while the dose corresponding to the figure for minimum lethal concentration for forty-eight hours' treatment (1:250,000) is only 0.4γ.

Rate of heart-beat in isolated fragments is profoundly stimulated by proflavine. The threshold for heart-beat inhibition and growth or cell-movement inhibition are strikingly different, for 10-day chick-heart explants are just capable of beating for forty-eight hours in a 1:10,000 solution of proflavine—i.e., in a concentration ten times greater than that representing threshold level for growth inhibition.

III. Action on Macrophages

A study of the action of sulphonamide drugs on macrophages is of particular value in a number of ways. The macrophages are themselves intimately concerned in the process of wound healing. The cells to be studied are taken from an adult organism. In culture, embryo extract and a plasma coagulum can be dispensed with: macrophages thrive and multiply actively in dilute serum. Conditions are thus more closely akin to those *in vivo* than is generally the case with tissue culture. Here as elsewhere, however, the conditions under which the cells are tested *in vitro* are more severe than they are in clinical application.

Pure cultures of macrophages prepared by Baker's (1933) technique from adult hen blood form a unicellular layer of isolated individuals clinging to the bottom of the ordinary D-type Carrel flask. These blood macrophages or "monocytes" are morphologically and functionally indistinguishable *in vitro* from the so-called tissue macrophages (Carrel and Ebeling, 1926; Jacoby, 1938). Attached to the flask they can be kept alive and multiplying for months under repeated feeding with 1 ml. of 20 to 40% blood serum in Tyrode per flask. Cultures were used for experiments after not less than eight days' cultivation in this basic medium.

In some preliminary experiments the cells were treated for seven days with somewhat dilute solutions of the appropriate drug mixed with serum. The range of concentrations used was: sulphanilamide 1:1,500→1:5,600, sulphathiazole 1:1,600→1:5,600, sulphapyridine 1:2,700→1:9,200. The experimental medium was replaced once, on the third of the seven days of treatment. Under these conditions the macrophages remained outstandingly healthy, showing a range of variation in morphological appearance not distinguishable from that of control cultures.

Detailed quantitative records of mitotic activity, accompanied by morphological studies, were then made by serial photography according to the technique described in Section I. In normal cultures (Jacoby, 1937a) feeding with serum in Tyrode brings about, after a *latent period* lasting from twenty to twenty-four hours, a *major wave* of mitotic activity reaching a peak between the thirtieth and the fortieth hour. Less regularly, the major wave is followed by a *minor wave* with a peak between the fiftieth and the sixtieth hour, after which the cells gradually return to quiescence. The whole period represents a single growth cycle, the end of which is taken as zero time. At zero time the drugs dissolved in 40% serum were applied and left in contact

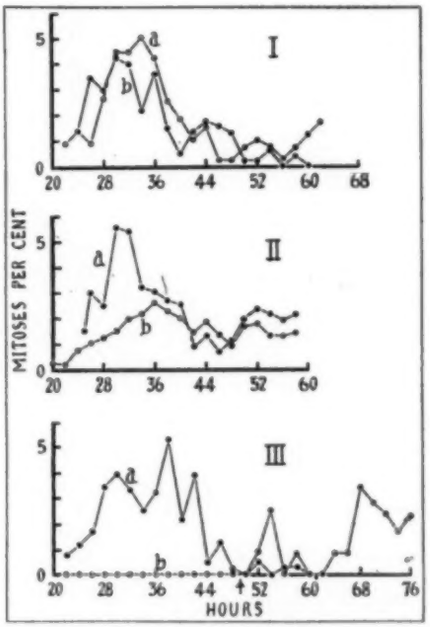

CHART II.—The action of sulphonamide drugs on adult hen-blood macrophages: the percentage of cells undergoing mitosis per hour, averaged over 2-hour periods (vertical axis), as a function of the time of incubation (horizontal axis). Except in iii *b*, where the arrow indicates the time at which the drug solution was replaced by normal feeding fluid, the drugs dissolved in 40% serum were in contact with the cultures throughout the period recorded. The normal latent period of about 20 hours is not included in the graphs.

(i) *a*, Sulphapyridine 1:3,400; *b*, sat. sol. (1:800 approx.).

(ii) *a*, Sulphathiazole 1:2,300; *b*, average curve of 1:1,000 and sat. sol. (1:500 approx.).

(iii) *a*, Sulphanilamide 1:2,300; *b*, 1:500.

with the cells for a whole growth cycle—except where strong inhibition was obvious, in which case the experimental fluid was replaced by fresh dilute serum after forty-eight hours or sooner (Chart II, iii, *b*). Serial photography was started towards the end of the normal latent period and carried on for the next forty to fifty hours so as to cover the main phase of the growth cycle. The percentage mitoses per hour were determined and plotted as the average of two-hour periods.

At the lower range of concentrations referred to above, analysis by this method (Chart II, i, ii, iii, *a*) did not reveal any depressant effect on mitosis; and phagocytosis of disintegrating by normal cells—a process already known from normal cultures (Jacoby, 1937b)—was repeatedly observed. These *a* curves can thus be conveniently used to illustrate normal growth under serum feeding.

It was then found that the drugs were considerably more soluble in serum than in Tyrode (see table), and

use was made of this fact by *directly* dissolving weighed quantities of the drugs in 40% serum at 39° C. for twenty-four hours. Concentrations were thus reached which

Table showing Solubility of Sulphonamide Drugs in 40% Hen Serum and in Tyrode's Solution. Figures are mg. per 100 c.cm.

	Sulphanilamide	Sulphathiazole	Sulphapyridine
40% serum at 39° C. ..	1,600	200	125
Tyrode at 39° C.	1,380	85	50

should be similar to those in wounds to which the powdered drugs are applied. At this higher range of concentrations (Chart II, i, ii, iii, *b*) certain interesting distinctions appeared, which may be summarized as follows:

Sulphapyridine.—The saturated solution in 40% serum (1:800 approx.) had almost no inhibitory effect within the growth cycle recorded (Chart II, i, *b*). The cells remain normal in appearance and in phagocytic activity; they move and divide in the neighbourhood of crystals.

Sulphathiazole.—At 1:1,000 or 1:500 (saturated solution) in 40% serum (Chart II, ii, *b*) the size of the major mitotic wave is somewhat reduced, although mitosis still remains vigorous. Certain morphological changes, however, persist during the entire period of application, and indicate a toxic effect of the drug: the cells round off as spheres or disks and become filled with a fair number of fat granules, while amoeboid movement is largely suppressed (Plate, Fig. 1). Within one or two days of replacing the experimental medium with fresh serum, normal morphology and growth are restored (Fig. 2).

Sulphanilamide saturated in 40% serum (1:60 approx.) and also at 1:100 causes disintegration and death of the cells. From a twenty-four-hours' application there was no recovery on feeding with fresh serum. These results do not exactly agree with those from fibroblasts reported in Section I; but differences in cultural conditions, in the size and distribution of the cell populations, and perhaps chiefly in the duration of drug treatment may account for this discrepancy.

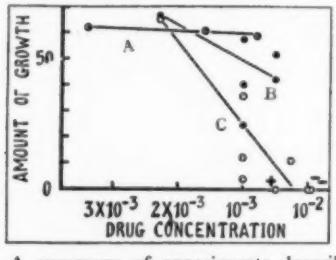

CHART III.—A summary of experiments described in Section III: the amount of growth between the 23rd and 48th hour, expressed as the sum of hourly percentages of mitosis (vertical axis), as a function of drug concentration (horizontal axis).

+ = Recovery in fresh serum; − = No recovery in fresh serum.

A = sulphapyridine; B = sulphathiazole; C = sulphanilamide.

In concentrations of 1:250 and 1:500 cell activity, particularly multiplication, is almost completely suppressed (Fig. 4), but on replacing the drug medium with fresh serum, normal growth is restored (Chart II, iii, *b*). In 1:1,000 similar gross inhibition was sometimes seen, while in other instances there was merely a prolongation of the normal latent period of twenty to twenty-four hours to thirty-six hours or more. This was followed by a marked mitotic response, during the course of which the morphological appearance of the cells, initially similar to that in higher concentrations of sulphathiazole, underwent a *spontaneous recovery* while still under the influence of the drug. Only a certain accumulation of fat granules persisted in the cells (Fig. 3). Again, recovery was quick and complete on feeding with fresh serum (Fig. 5). Phagocytosis was not observed in sulphanilamide cultures at a concentration of 1:500 or higher.

These results indicate that the relative toxicity of the three sulphonamides is the same for macrophages as for fibroblasts. A fact of particular interest is that while at equal concentrations sulphanilamide inhibits the division of macrophages much more strongly than sulphathiazole, the latter produces more pronounced and persistent morphological changes indicative of impaired cellular vitality. In so far as the comparatively small number of these lengthy experiments makes possible, the results are summarized in Chart III, in which the amount of growth between the twenty-third and forty-eighth hours, expressed as the sum of the hourly percentages of mitosis, is plotted against the concentration of the drugs.

Proflavine was also tested on these macrophages. In a final concentration as low as 1:1,000,000 in 30% serum applied for twenty hours it caused complete disintegration of the cultures.

LEGENDS FOR THE SPECIAL PLATE

FIGS. 1-5.—Illustrating the action of sulphathiazole and sulphanilamide solutions on cultures of adult hen-blood macrophages. × 165.

FIG. 1.—Three days after the application of 1:1,000 sulphathiazole in 40% serum. Rounding off of the cells with fat accumulation.

FIG. 2.—The same culture: complete recovery following the replacement of the drug solution by fresh serum.

FIG. 3.—Three days after the application of 1:1,000 sulphanilamide in 40% serum. A partial recovery has taken place spontaneously, but a certain amount of fat remains.

FIG. 4.—Twenty hours after the application of 1:500 sulphanilamide in 40% serum. Inhibition is evident: the cells are small and shrunken.

FIG. 5.—The culture illustrated in Fig. 3, showing complete recovery from the action of 1:1,000 sulphanilamide for 3 days when the drug solution is removed and replaced by fresh serum.

FIG. 6.—Multilayered sheet of mixed epithelium and mesenchyme from the lung of the embryonic chick. The epithelial sheet has completely invested a collection of crystals of sulphadiazine lying in saturated solution in the culture medium at 37° C. Note the tendency of the epithelium to use the solid structure provided by the crystals as a support. × 120.

FIG. 7.—Chick-heart fibroblasts from a fresh explant threading their way through crystals of sulphapyridine lying in saturated solution in the culture medium at 37° C. Cells are normal in size, amoeboid activity, and refringence, but show a slight tendency towards vacuolization. × 120.

IV. Action on Epithelia

The growth of epithelia *in vitro*, while it may be prolonged and abundant, is much less regular and predictable than that of mesenchyme cells, and no satisfactory method for the quantitative analysis of their growth has yet been devised. The surface of the plasma coagulum is used, following the prescription of Ebeling (1924), and in the case of fibrinolytic epithelia it is desirable to wet the surface of the hardened coagulum with a saline solution of the drug at the appropriate concentration. This is done by applying the solution with a pipette over the whole surface of the clot and then removing it so far as is possible. The test tissues used were 10-day chick-embryo intestine and lung and late rat-embryo kidney. The results for the four drugs considered in Section II may be summarized as follows. Inhibition to fibroblasts and epithelia from a common source proceeds *pari passu*, and there is no indication of differential toxicity favouring one type or the other. Either epithelial sheets and fibroblasts grow together or neither grow. The concentrations at which lung and intestinal epithelia from the 10-day-old chick are just able to grow for twenty-four to forty-eight hours *in vitro* are not closely defined, but they may be reasonably approximated to the figures already quoted as threshold concentrations for the inhibition of 10-day chick-heart fibroblasts (1:150 and 1:500 approx. for sulphanilamide and sulphathiazole

G. GREGORY KAYNE: EARLY BRONCHOGENIC TUBERCULOSIS

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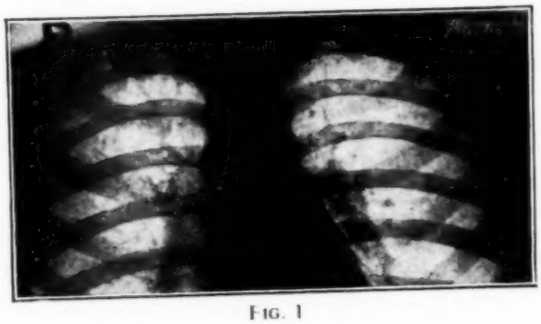


FIG. 1

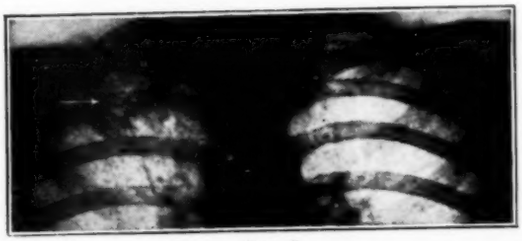


FIG. 2

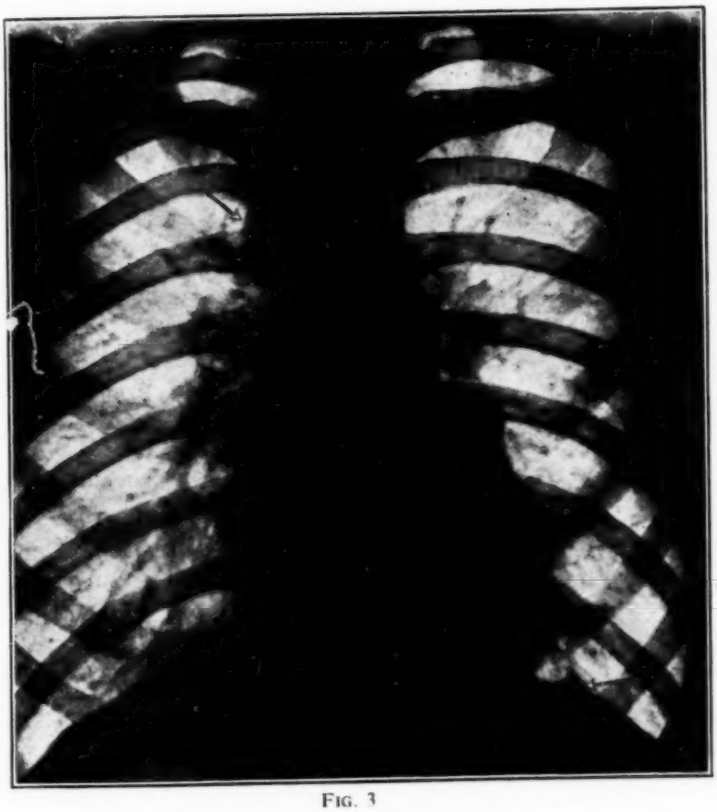
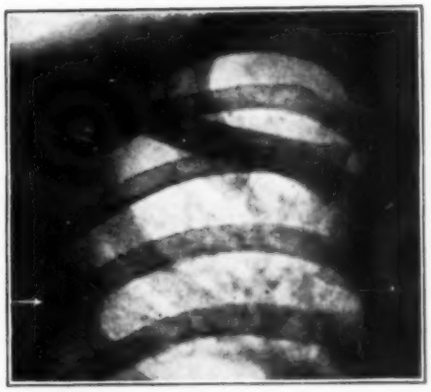


FIG. 3

FIG. 4

FIG. 5



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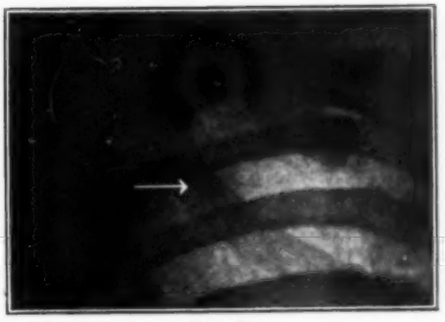

FIG. 7

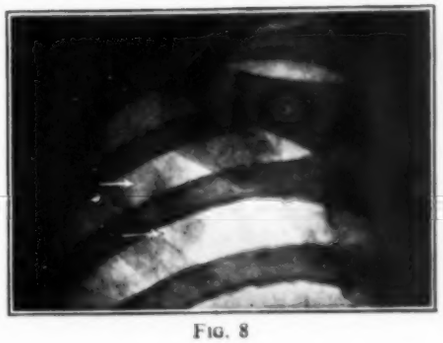

FIG. 8

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(For legends see text)

FIG. 1

FIG. 2

FIG. 3

FIG. 4

FIG. 5

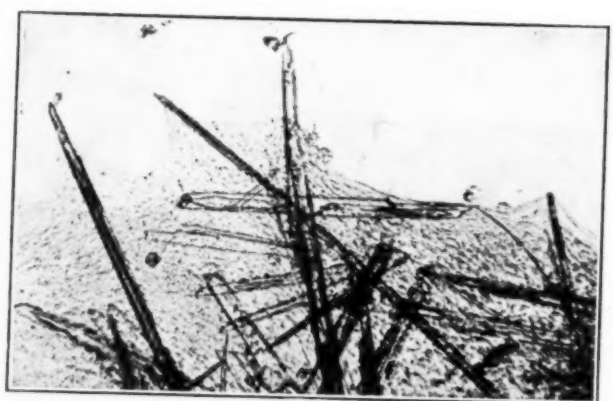

FIG. 6

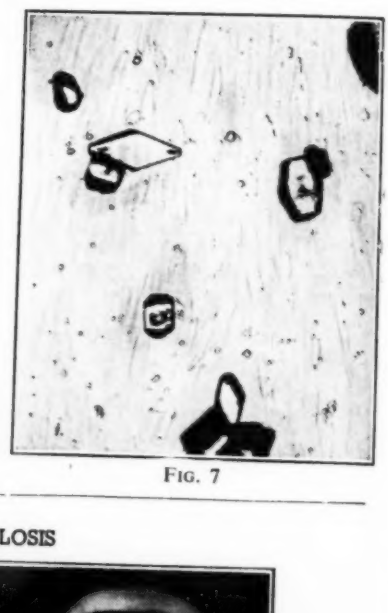

FIG. 7

G. GREGORY KAYNE: EARLY BRONCHOGENIC TUBERCULOSIS

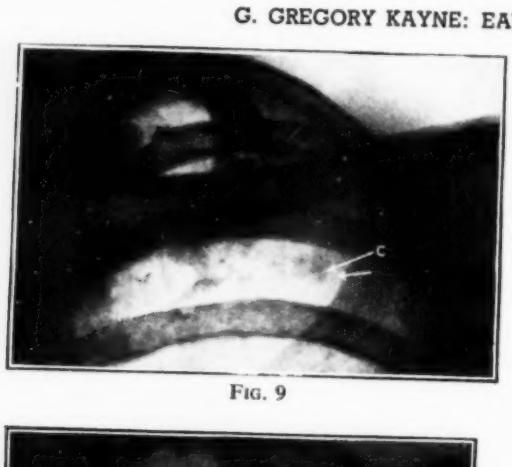

FIG. 9

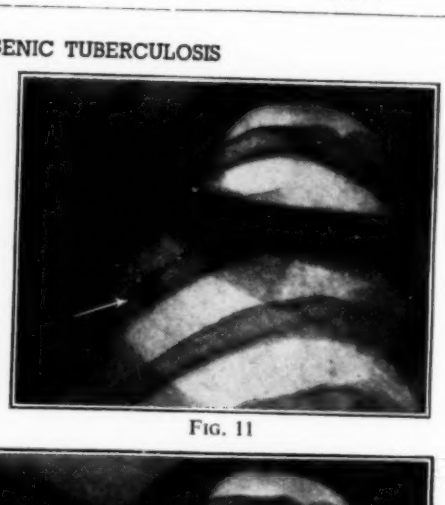

FIG. 11

FIG. 10

FIG. 12

respectively). Epithelial sheets which occasionally spread in higher concentrations of sulphanilamide rapidly undergo maceration into separate cells.

A striking feature of these experiments is the ease with which epithelial sheets grow among and invest crystals of sulphapyridine and sulphadiazine lying in saturated solution in the culture medium. Needles of recrystallized sulphadiazine, for instance, act as a support for the growing cells; they tend to become completely invested by an epithelial sheet, forming a tent for which the crystal acts as tent-pole (Fig. 6). In short, it is in the highest degree unlikely that under the less stringent conditions of application *in vivo* either of these drugs could retard the new growth of epithelia over a raw surface.

Proflavine likewise shows no power of differential inhibition. The concentration which just permits the spread of epithelia from the intestine of the 10-day-old chick lies between 1:100,000 and 1:120,000.

Discussion

At the present time no method of analysing the general toxicity of drugs to living cells has been devised which combines the accurately controlled and detailed observations of tissue culture with conditions directly comparable to those under which the drugs are applied clinically. Owing to the absence of a circulatory system and of the detoxicating mechanisms of the organism as a whole, tissue culture tests are more stringent than clinical ones—a fact partly counterbalanced by the greater resistance of embryonic tissues to inhibition of their growth. This reservation can hardly apply, however, to the experiments on "adult" cells described in Section III.

The experiments described above, independently performed on a variety of cell types, are consistent among themselves in the sense that they rank the drugs considered in the same order of *effective* toxicity, while the *order of magnitude* of the significantly inhibitory concentration is found to be the same throughout. The results are in accord with somewhat less detailed observations by Wolff and Julius (1939) on sulphanilamide. Comparison of the drugs at equal concentrations shows sulphathiazole to be the least favourable, in view of the wide range of concentration over which it is appreciably inhibitory and of its pronounced effect on the morphological appearance of macrophages; but the effective toxicity—under the conditions of direct application which were envisaged in these experiments—is determined by relative solubility, and falls into the decreasing order: sulphanilamide→sulphathiazole →sulphapyridine and sulphadiazine. Studies on red or white blood cells by Fleming (1938), Osgood (1938), and Bullowa *et al.* (1940) tend towards the view that sulphanilamide is feebly toxic in high concentrations, while sulphapyridine is completely non-toxic. The action of various drugs on brain tissue has been recorded by Russell and Falconer (1940a, 1940b): powdered sulphanilamide and sulphapyridine produce no specific reaction, while 0.1% proflavine at *p*H 6.2 is hardly more harmful than neutral saline. The second of these observations contrasts sharply with the toxicity of proflavine as determined by tissue culture tests. Proflavine appears in these as a highly toxic substance, the order of magnitude of the significantly inhibitory concentration being 10^{-5} or 10^{-6}.

The experiments described above give one no ground for believing that the sulphonamide drugs *accelerate* growth, though such an action might be brought about indirectly by suppressing the inhibitory action of infective organisms (Levaditi *et al.*, 1940). They do not exclude the possibility that sulphanilamide and sulphathiazole in particular may exert an inhibitory effect on wound healing, however transient (as Bricker and Graham, 1939; Jeffrey, 1940; Veal and Klepser, 1941, have found for sulphanilamide). Colebrook and Francis (1941) do not, however, find that sulphanilamide exerts an appreciable inhibitory effect when dusted on to superficial wounds, and Taffel and Harvey (1940) have not been able to confirm the observations of Bricker and Graham. The most striking feature of the tissue-culture studies described above is the remarkably feeble inhibitory action upon tissue cells of *all* the sulphonamide drugs considered. There is a *profoundly significant difference* between the thresholds for bacterial and cellular inhibition in all three cases. In short, the evidence from tissue cultivation is that in choosing between one sulphonamide drug and another for direct application to wounds their relative effects on tissues *can be disregarded in favour of their relative specific bactericidal powers.*

Summary

The treatment of infected wounds by direct chemotherapy with sulphonamide powders justifies a detailed analysis of the action of these drugs on living cells.

The effects of sulphanilamide, sulphathiazole, sulphapyridine, and (in some tests) sulphadiazine on fibroblasts, macrophages, and epithelia have accordingly been tested by a number of different cultivation techniques.

The drugs were applied in concentrations ranging from saturation strength downwards, and for periods lying between fourteen hours and three days.

Compared at equal concentrations, sulphathiazole is the most toxic of these drugs.

The effective toxicity under the conditions of clinical application is, however, determined by the relative solubility of the drugs, and falls into the decreasing order: sulphanilamide→ sulphathiazole→sulphapyridine and sulphadiazine.

The growth inhibition and unfavourable morphological effects produced by the highest concentrations of sulphathiazole are followed by complete recovery on removal of the drug. Cells are not capable of withstanding prolonged subjection to the highest concentrations of sulphanilamide, but recovery readily takes place from concentrations of 1:150 downwards. Neither sulphapyridine nor sulphadiazine inhibits significantly in saturated solution at body temperature.

The feeble inhibitory action of the sulphonamide drugs is favourably contrasted with that of proflavine.

Attention is called to the profound difference between bacteriologically effective concentrations and those which are appreciably toxic to cells.

It is therefore suggested that in the choice of sulphonamide powders for direct application to wounds their relative specific bactericidal power should outweigh other considerations.

We wish to thank Colonel L. Colebrook, Dr. F. H. K. Green, and Dr. F. Hawking for their helpful advice and criticisms.

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ORIGIN, DIAGNOSIS, AND MANAGEMENT OF EARLY BRONCHOGENIC TUBERCULOSIS

BY

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(WITH SPECIAL PLATE)

There is scarcely a report by a medical officer of health, tuberculosis officer, or sanatorium superintendent that does not refer to the advanced stage of the disease in which those suffering from pulmonary tuberculosis first come for treatment under the tuberculosis scheme. The cry is, "If only we could get the cases early!" The emphasis laid on this plea implies that if people were seen early in the development of the disease transmission of infection to others would be avoided and the disease would be made to heal in all patients. It is not surprising, therefore, that some advocates of mass radiological examinations see in them the key to the control of tuberculosis. This should not, however, be taken for granted, because up to the present relatively few such early cases have been detected, treated, and followed up; indeed, no clear-cut conception of what constitutes an early case is being taught.

Definitions

The term "pulmonary tuberculosis," itself requires clarification. It usually refers to the disease commonly seen in adolescents and adults, characterized by gradual destruction of the lungs as a result of the intrabronchial spread of massive doses of bacilli following cavitation of a tuberculous focus. But other active tuberculous lesions are common in the human lung—those of the primary infection and of the dissemination that follows it. It would be well, therefore, to use the term "pulmonary tuberculosis" as implying any active lesion in the lung belonging to any phase in the evolution of tuberculosis, and to restrict the use of another term—that of "bronchogenic tuberculosis"—to the common type of bronchogenic disease.

In discussing the early stage of bronchogenic tuberculosis mention must be made of those lesions in the lung which occur during the phase of dissemination in the evolution of tuberculosis (Kayne, Pagel, and O'Shaughnessy, 1939) (of which chronic miliary tuberculosis is but one clinical type), for such haematogenous cases may simulate bronchogenic tuberculosis when the lesions cavitate (Case 1). These thin-walled "punched" cavities have, however, little caseous matter in their walls and probably only rarely lead to intrabronchial transmission of bacilli. The common beginning of bronchogenic tuberculosis is a single focus, usually in the upper part of the lung, which enlarges, liquefies, and cavitates, when secondary foci develop as a result of intrabronchial transmission (this process has been accurately reproduced in animals). Since the disease takes on its grave aspect with liquefaction and cavitation of the first focus, early bronchogenic tuberculosis must be defined as the earliest recognizable caseous focus which has not yet opened into a bronchus. Such a focus does not give rise to abnormal physical signs, is often associated with no symptoms, either local or constitutional, and may even present no evidence of toxaemia as shown by a raised sedimentation rate or altered blood picture. But it can be detected in a radiograph of good quality when it is less than a quarter of an inch in diameter unless the focus is entirely hidden by the shadow of a bony structure. It may appear as a uniform cloudy haziness or as a group of nodules, some of which coalesce. To summarize, early bronchogenic tuberculosis is the smallest radiologically detectable focus with potentialities for liquefaction.

A small shadow in the upper part of the lung field may be caused by other tuberculous lesions (active or healed). Thus the pulmonary focus of an active primary infection may sometimes be seen as a distinct shadow in the lung field. Nowadays the primary infection occurs often during adolescence and not very rarely even in adults, but, as in children, enlargement of at least the corresponding hilar shadow is then seen—a change not met with in the early lesion of bronchogenic tuberculosis. Again, the pulmonary foci of dissemination associated with and following the primary infection may resolve completely, or may leave behind a few tiny nodules scattered throughout the lungs, or a group of rather bigger nodules at the apices (Simon foci), or one or more larger foci a quarter of an inch or more in diameter. The latter foci usually consist of a caseous centre with fibrotic capsule, and have been termed "round foci." Finally, quite sizable lesions of bronchogenic tuberculosis may develop and heal unsuspected, so that one is presented with a single residual non-active focus which may be mistaken for a first or early focus of bronchogenic tuberculosis.

LEGENDS FOR THE SPECIAL PLATE

FIG. 1.—Case 1 (May 31, 1939). Coarse miliary mottling in upper half of each lung.

FIG. 2.—Case 1 (June 11, 1940). In addition there is now a thin-walled irregular cavity in right upper zone.

FIGS. 3 and 4.—Case 2. Showing progression towards bilateral cavernous bronchogenic tuberculosis (films taken in August, 1939, and November, 1940).

FIG. 5.—Case 3. Round focus with calcified shell in left infraclavicular region.

FIG. 6.—Case 4. Primary calcified complex on left side (not reproduced) and roundish lesion in right mid-zone.

FIG. 7.—Case 5 (March 13, 1940). Faint circular shadow on right in fourth posterior interspace, and "filling" of right costo-phrenic angle (not reproduced).

FIG. 8.—Case 5 (November 4, 1940). Showing definite extension of shadow upwards and outwards.

FIG. 9.—Case 7. Roundish focus in left infraclavicular region with two tiny calcifications (marked C).

FIG. 10.—Case 7. Showing definite increase in size of shadow, six months later.

FIG. 11.—Case 9 (January, 1940). Calcified foci on both sides, with pleural thickening at left base (right upper zone only reproduced).

FIG. 12.—Case 9 (December, 1940). Showing a faint but definite shadow around a group of small calcified foci on right side.

Origin of Bronchogenic Tuberculosis

The early lesion of bronchogenic tuberculosis occurs in an individual who has already overcome his primary infection, though the interval between the onset of the first infection and the lesion of bronchogenic tuberculosis may be as short as a few months (Case 2). There are several possible theories of the origin of the early lesion, since it is known that bacilli may remain alive in an apparently healed primary pulmonary focus (rarely), a primary glandular focus (more commonly), and in foci of dissemination (quite commonly). As a result of lowering of resistance or fol-

* The views expressed in this paper are those of the author, and do not necessarily represent those of the Middlesex County Council.

lowing a contiguous non-tuberculous process, exacerbation might occur in any of these foci, which could themselves liquefy and cavitate, or, if the exacerbation occurs in the neighbourhood of a small bronchus, the discharge of a large number of bacilli into another part of the lung might give rise to a fresh focus, which would cavitate in due course. Neither of these alternatives seems to happen in the case of the primary pulmonary lesion, but both have been shown conclusively to occur in connexion with the remains of haematogenous disseminations. The apical remains (Simon foci) exacerbate and give rise to infiltrations lower in the lung, which may liquefy and cavitate; and "round foci" exacerbate and themselves cavitate. Another possibility is a new focus that develops as the result of a fresh exogenous infection. No pathological confirmation of this is available, but epidemiological and clinical evidence points strongly to its occurrence. Presumably a focus develops when massive and repeated doses of bacilli are inhaled. The lesion probably regresses spontaneously unless at the same time resistance has been lowered, when the lesion tends to progress to bronchogenic tuberculosis. Yet another possibility for which supporting evidence is scarce is superinfection. The mechanism would then be as follows. The introduction of a fresh massive dose would not itself give rise to a new focus in the lung, but the destruction of the bacilli so introduced would release toxins which could cause exacerbation of healed primary or disseminated foci.

To summarize, it may be stated with some assurance that the two common mechanisms from which arises the early lesion of bronchogenic tuberculosis are exacerbation of residual foci of dissemination and fresh exogenous reinfection with massive doses in people with lowered resistance, but the relative frequency of these two mechanisms cannot be established at present. A third, uncommon, origin is a bronchogenic sequel to a progressive chronic dissemination in the lungs.

Detection of Early Bronchogenic Tuberculosis

It is again stressed that early bronchogenic tuberculosis can be detected only by radiological examination. Evidence for this will be found in the work of Braeuning in Stettin and of Malmros and Hedvall in Lund, both of whom published monographs in 1938 on their findings in students, nurses, and hospital personnel. Braeuning reported on 86 people who presented an abnormal radiological picture within one year or less of having given a normal radiograph; primary infection as a cause of the abnormal shadows seen in the later radiographs could be excluded with reasonable certainty. In no fewer than 50 of the 86 persons no symptoms whatever could be elicited. In 10 of the 86 the interval between a clear radiograph and the development of a focus was not more than three months, so that the question of symptoms could be examined with special care; in no fewer than 6 there were no symptoms whatever. Similarly, in the majority of 43 students and nurses who were tuberculin-positive and gave an abnormal radiograph after an interval following a normal one, Malmros and Hedvall found that the onset of the radiological shadow was not accompanied by symptoms.

It is clear that early bronchogenic tuberculosis will not be detected if one waits until the individual consults his doctor, that it can only be discovered by mass radiological examination of the apparently healthy, and that the most fruitful results will be obtained in those exposed to massive infection or conditions lowering general resistance, such as home and work contacts, medical students, nurses, industrial employees, etc. The method to be used requires careful consideration. If such examinations are merely for the purpose of detecting well-developed bronchogenic tuberculosis in people who delay consulting a doctor or in whom the doctor fails to recognize this possibility, then any method will do, including miniature radiography and screening. If, however, the mass examination is intended to detect the early focus of bronchogenic tuberculosis, then two conditions are essential—a good radiograph, and repetition of the examination every six months or so; for it is most desirable to have a normal film to compare with, and too long a delay between examinations may allow cavitation to occur before the recently developed focus had been detected.

Diagnosis of Early Bronchogenic Tuberculosis

The recognition of a radiological shadow as one of early bronchogenic tuberculosis is easier if a radiograph and a tuberculin-test result, dating no further back than a few months, are available. When a previous film is not available the shadow must be differentiated from a primary pulmonary focus, Simon foci, round foci of dissemination (Cases 3 and 4), and the healed residua of previously unsuspected bronchogenic tuberculosis. It has been shown that the focus of early bronchogenic tuberculosis is found as often above the clavicle as below it, and that it appears as a group of small foci or a shadow with denser nodules in it as often as in the form of a homogeneous cotton-wool shadow. In the light of recent work the distinction (stressed by the late Fishberg, for instance) between a very benign apical tuberculosis and an acute progressive infraclavicular *Frühinfiltrat*, or "early infiltration" (as worked out by Assmann and Redeker), is no longer tenable. In practice what needs to be decided is whether the radiological shadow represents an active lesion. It has already been stated that there may be total absence of symptoms. There may be slight pyrexia; but Braeuning found that in 24 of 43 patients, in whom axillary temperature was recorded several times a day, no pyrexia could be detected. Similarly, in 42 of 75 patients in whom the sedimentation rate was noted the figure was normal, and this series included some patients with early lesions which rapidly cavitated. Again, 7 of 48 patients with definitely active lesions showed a perfectly normal blood picture. Only in a few of his patients were all these three investigations carried out, but in 3 of them they were normal. Similarly, Malmros and Hedvall conclude from their findings in 43 students and nurses that whether the focus begins as a group of small nodules or as a so-called "early infiltration" the sedimentation rate is generally not raised. It appears, therefore, that help in deciding whether the lesion is active or not must often be obtained by noting changes in the radiological shadow after an interval (Cases 5, 6, and 7).

A month seems a suitable interval, since this would generally allow enough time to produce a radiological change, and would as a rule, but only as a rule, not be long enough to allow gross harmful changes to develop, unless the case is already one of those which deteriorate rapidly even under treatment.

As will be shown later, another film after a short interval is also of great help in the management of the case. But if one is to rely on these slight radiological changes the standard technique of the films must be good and uniform, and changes that might be caused by technical differences must be carefully appraised.

Prognosis and Management

An attempt must next be made to estimate the outlook for the lesion. Serial radiographs will have already given some indication of its rate of progression. It will be of immense value to know whether the lesion developed as

a result of lowered resistance and exacerbation of old foci or as a new exogenous infection from massive contact with or without lowering of resistance. When only massive contact is a factor, interruption of this may be sufficient to allow natural regression of the lesion* (Case 8). If lowering of resistance is a factor, then clearly this will not be enough, and measures to increase this resistance, either in the home or in a sanatorium, will need to be taken. It may be very difficult or even impossible to find the incriminating factor or factors, but careful history-taking and investigation of the patients' environment should discover this with reasonable sureness in an important proportion of cases.

The first steps in the management of the individual patient are therefore serial films and investigation of aetiological factors. If the lesion is only doubtfully progressive, or is probably due to massive contact alone which can be interrupted, then it may be justifiable to allow the patient to carry on with his work, more rest in leisure hours being suggested, and monthly investigations with radiographs, sedimentation rates, etc., being continued. If the lesion is definitely progressive, and the factor of lowered resistance cannot be excluded, more is indicated. Before advising institutional treatment, measures short of this must be considered, because reluctance to give up work and leave home for several months is likely to be very great when the patient feels there is nothing the matter with him. When ceasing work is likely to be followed by the necessary restful conditions, good food, and discipline in the home or with relatives, then this home treatment might be tried in the slowly progressive case, provided monthly radiographs and other investigations are practicable. Failing this a stay in an institution is essential.

A digression on tubercle bacilli in the sputum is here necessary. The definition of early bronchogenic tuberculosis excludes radiologically detectable cavitation, but even a tiny focus, if situated in the neighbourhood of a small bronchus, would produce a slight amount of bacilli in any sputum expectorated, even if cavitation had not occurred, and therefore the presence of bacilli in the sputum does not necessarily remove the case from the group of early bronchogenic tuberculosis. On the other hand, the outlook for such a patient is worse, because extension to other parts of the lung is already possible. It may be that even among people with early foci who produce no sputum, bacilli would be grown from the gastric contents of some or many; this requires further investigation. In the American classification of pulmonary tuberculosis "minimal lesions" are defined as: "(*a*) slight infiltration without demonstrable excavation; (*b*) a small part of one or both lungs—total volume of involvement, regardless of distribution, shall not exceed the equivalent of the volume of lung tissue which lies above the second chondrosternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side"; tubercle bacilli may be present or absent. The official classification in this country is so antiquated that it still relies on physical signs and does not appear to recognize the existence of radiography: discussion of it is therefore futile. The presence or absence of tubercle bacilli in association with the early lesion will clearly affect the management of the patient. Thus, to begin with, their presence will indicate institutional treatment in every case.

Institutional treatment may consist of sanatorium regime alone, rest in bed, or rest in bed combined with collapse therapy; bed rest, continued until the lesion is quiescent, should be considered a *sine qua non* of properly conducted collapse therapy. Whatever benefits may be claimed for sanatorium regime alone, this is not justified in the cases discussed here, because it is so vital that the institutional stay of these patients, most of whom feel more or less well and are reluctant to give up work and most anxious to return to it, should be as short as is compatible with safety. When there is no sputum, or no tubercle bacilli can be detected in the sputum (culture being of course employed), strict rest in bed, continued until there is evidence of quiescence as demonstrated by serial radiographs, sedimentation tests, and blood examinations, is sufficient unless the lesion shows signs of progression. If progression is evident at the end of a month's bed rest, or if there is no definite evidence of regression at the end of, say, two months, then continued bed rest alone is not justified. And to these patients, as well as to those whose sputum is positive, collapse therapy should be applied without delay. There is plenty of authoritative opinion to support this conclusion. Thus the following among American workers may be quoted: O'Brien (1933), Myers and Levine (1935), and John Alexander (1937). O'Brien favours phrenic interruption, permanent or temporary, according to the case. Turner and Collins (1936) show that artificial pneumothorax in these minimal cases is associated with very slight operative risk, that the percentage of cases with a free pleural space and therefore with an effective collapse is very high, and that the results are distinctly worse when the induction of a pneumothorax is delayed even by a few weeks. The general application of pneumothorax therapy for early bronchogenic tuberculosis does imply, however, that the treatment will be carried out both in institution and in clinic by experienced practitioners, or at least under their close supervision, and, if at all possible, by one physician throughout—the one who induced the pneumothorax.

Advice in regard to the treatment of early bronchogenic tuberculosis may thus be summarized: Get on with it at the beginning of the treatment, for as often as not it is the patient and not the physician who decides when it will end.

Mass Radiological Examinations

Unless the early cases of bronchogenic tuberculosis are properly managed and treated, little benefit will accrue from mass radiological examination: 15% of Braeuning's patients were sputum-positive within one year of a normal radiograph; 41% became sputum-positive within a short time of detection. A cavity was visible after a normal radiograph in 1 case within a month, in 7 within six months, and in 15 within a year. (Hence the importance of repeated radiographic examination at intervals of less than a year if infection from open cases to others is to be prevented.) Death took place from the time of a normal radiograph in 1 case within a month, and in 2 within fourteen months. In most cases, however, the development of the disease was slow at first.

From this it appears that while mass radiological examination will be of distinct benefit to individuals and will result in decreasing infection to others, as a method of eradicating tuberculosis it is likely to play a truly effective part only under the following conditions:

1. That the examinations will be carried out extensively.
2. That the method of radiological examination used will be the best available—that is, radiographs will be taken with a satisfactory technique.
3. That re-examinations will be carried out at no longer interval than six months or so.
4. That full facilities will be available for detailed investigation and observation of all cases with an abnormal or suspicious radiograph.
5. That all persons shown by this means to be suffering from early bronchogenic tuberculosis will have proper and adequate institutional treatment.
6. That such treatment will not interfere with the return of the patient to his work and with the economic security of the family during the absence of the breadwinner, housewife, or mother.

To secure these conditions in full would probably necessitate economic and social changes in our community that

* Persistent massive contact in such a case might be harmful not only by influencing this lesion but by giving rise to a fresh lesion which would progress if resistance were subsequently lowered.

would themselves do more than mass radiological examinations to reduce the incidence of tuberculosis.

Case Reports

Case 1.—A girl aged 8. Mother suffers from advanced bronchogenic tuberculosis. Tuberculin-positive; no symptoms; radiograph on May 31, 1939 (Special Plate, Fig. 1), showed coarse miliary mottling in upper half of each lung. Child not seen again till June 11, 1940, when she was stated to be well and had put on 10 lb. There was tiredness, however, and a radiograph (Fig. 2) showed in addition to the miliary mottling a thin-walled irregular cavity in the right upper zone, presumably due to coalescence and liquefaction of some of the larger foci.

Case 2.—A lad aged 16. Seen in a hospital in February, 1939, for unexplained fever: a radiograph on February 15 showed no abnormality, but one taken a week later revealed an opacity to right of superior mediastinum, and the tuberculin test was positive. Diagnosis: primary tuberculous infection with involvement of mediastinal glands. April 12: lymphocytic left pleural effusion; mediastinal shadow smaller. April 25 to June 7: in sanatorium. Radiograph on August 16 (Fig. 3) still showed enlargement of right paratracheal glands and remains of pleurisy at left base. Radiographs November 15 and January 31, 1940, revealed fresh foci at top of left apex, apparently unchanged in this interval, there being no symptoms, and sedimentation rate (S.R.)—Westergren 1 hour—remaining normal. Radiograph July 31 (Fig. 4) showed bilateral bronchogenic tuberculosis with cavitation. (Interval between onset of primary infection and fully developed bilateral cavernous bronchogenic tuberculosis thus not longer than seventeen months.)

Case 3.—A man aged 32, referred by recruiting medical board. Mother suffers from advanced bronchogenic tuberculosis. No symptoms; radiograph October 15, 1940 (Fig. 5), showed round focus with calcified shell in left infraclavicular region; S.R. normal. Radiographs one month and three months later showed no change in appearances of this focus. (Diagnosis: "round focus" of dissemination; calcifying or partly calcified primary focus excluded, as no calcification seen in corresponding hilar glands.)

Case 4.—A girl aged 11. Father died of bronchogenic tuberculosis six years ago; now in contact with brother suffering from advanced bronchogenic tuberculosis. Slight cough; S.R. normal; radiograph, March 6, 1939 (Fig. 6), showed primary calcified complex on left side and roundish lesion in right mid-zone. Admitted to sanatorium for observation: tuberculin test found positive. Throughout stay there and after discharge, radiographs showed no change in appearances of this focus. (Diagnosis: "round focus" of dissemination; it is possible, however, that the focus represented an "early infiltration" which was already quiescent when the girl was first seen.

Case 5.—A woman aged 33. Intermittent contact until Christmas, 1939, with sister suffering from bronchogenic tuberculosis. History of pain in right side of chest in March, 1939, when she remained in bed for a month. No symptoms; S.R. = 15. Radiograph on March 13, 1940 (Fig. 7), showed faint circular shadow on right, in fourth posterior interspace and partly covered by anterior part of second rib, and "filling" of right costo-phrenic angle. April 15: no symptoms; S.R. normal; radiograph, apparently no change. September 10: no symptoms; S.R. normal; radiograph showed some change in shape of shadow. November 4: no symptoms, but had a "cold" a week before; radiograph (Fig. 8) now showed definite extension of shadow upwards and outwards; recommended for sanatorium. (Diagnosis: probably exacerbation of "round focus" of dissemination; note (1) the pleural effusion a year before first seen, (2) the interruption of contact.)

Case 6.—A girl aged 18. Father suffered from advanced bronchogenic tuberculosis (died October, 1940). November, 1938: no symptoms; radiograph showed infraclavicular shadow on left. February, 1939: no symptoms; radiograph, shadow unaltered. February, 1940: no symptoms; weight about the same; radiograph showed increase in size of focus. April, 1940: confessed to fatigue during past two months; no abnormal physical signs in chest; S.R. = 16; radiograph showed further increase in infraclavicular shadow. In sanatorium from May to August. September, 1940: no symptoms; radiographically, shadow was "harder" in appearance, indicating fibrosis. (Diagnosis—most likely sequence: (*a*) healed dissemination with residual small foci; (*b*) development of "round focus" which remained latent; (*c*) exacerbation of this focus due to ? superinfection and/or lowering of resistance.)

Case 7.—A man aged 25, referred by recruiting medical board. Two years previously radiographed at a tuberculosis dispensary elsewhere: this radiograph, inspected by me, revealed no abnormality in lung fields. First seen May 23, 1940: slight cough and sputum; radiograph (Fig. 9) showed roundish focus in left infraclavicular region with two tiny calcifications in one part of it; S.R. normal; sputum negative. June, 1940: very slight cough and sputum (negative); put on 2 lb.; S.R. normal; radiograph, apparently no change. August, 1940: no symptoms; very slight sputum (negative); lost 3 lb.; S.R. normal; radiograph, apparently no change. November, 1940: had a "cold" last week; slight cough and sputum; has put on 3 lb.; S.R. normal; radiograph (Fig. 10), when compared with film taken in May, showed definite increase in size of shadow. (Diagnosis: slowly progressive lesion, probably due to exacerbation tiny round healed foci of dissemination. This case also illustrates the cumulative effect of very small increases in size of radiological shadows.)

Case 8.—A girl aged 17. Mother suffers from advanced bronchogenic tuberculosis and admitted to sanatorium. June, 1939: no symptoms; radiograph showed shadow in right second anterior interspace. July, 1939: radiograph suggests decrease in this shadow. October, 1939: radiograph, shadow smaller and "harder" in appearance. (It was therefore concluded that the shadow on the first radiograph had represented an *active* focus of early bronchogenic tuberculosis.) December, 1939: no symptoms; working. March, 1940: no symptoms; radiograph shows the shadow originally seen replaced by a very few fibrotic strands and nodules. (Diagnosis: early bronchogenic tuberculosis ("early infiltration"), ? origin, regressing without treatment, contact having been interrupted; therefore presumably arose as the result of massive infection without lowering of resistance.)

Case 9 (This case, though not referred to in the text, is included because it is closely connected with the subject of this paper, as it shows the really early stage of a true "relapse").—A woman aged 28. Case diagnosed as pulmonary tuberculosis in 1934, when a radiograph showed "(R.) slight infiltration of upper zone, (L.) infiltration of upper and middle zones with cavity in upper zone"; later admitted to sanatorium, where a left A.P. was induced, which was carried on until December, 1937. Seen in November, 1938, May, 1939, and January, 1940, when on each occasion a radiograph (Fig. 11) showed the same appearances—calcified foci on both sides, with pleural thickening at the left base. When seen in December, 1940, she was feeling fit but had a slight cough; she had lost over 6 lb. since January, and had been working seven days a week; S.R. normal; radiograph (Fig. 12) showed a faint but definite roundish shadow around a group of small calcified foci on the right side. Note: (1) the calcified foci on the right side were not present in the film of 1934, so that they did not represent a healed dissemination, but healed lesions of bronchogenic tuberculosis; and (2) the group of foci around which the recent shadow is seen had themselves changed in appearance. This suggests the diagnosis of recent exacerbation, due to lowered resistance, of a "healed" focus of bronchogenic tuberculosis, the exacerbation having caused some of the calcified foci to be "ejected" or at all events to change in position.

Summary

It is suggested that the term "pulmonary tuberculosis" should be used as implying any active lesion in the lung belonging to any phase in the evolution of tuberculosis, and the use of the term "bronchogenic tuberculosis" be restricted to the common type of bronchogenic disease.

"Early bronchogenic tuberculosis" is defined as the smallest radiologically detectable focus with potentialities for liquefaction.

The two common mechanisms leading to the early lesion of bronchogenic tuberculosis are exacerbation of residual foci of dissemination and fresh exogenous reinfection with massive

doses in people with lowered resistance. Another, uncommon, origin is a bronchogenic sequel to a progressive chronic dissemination in the lungs.

Early bronchogenic tuberculosis is generally *not* associated with symptoms or signs (including sedimentation rate and blood picture), and can be detected only by radiological examination of the apparently healthy, particularly among groups exposed to massive infection or circumstances lowering resistance.

The focus of early bronchogenic tuberculosis must be differentiated from other tuberculous lesions: a primary pulmonary focus, apical Simon foci, "round foci" of dissemination, and the healed residua of a previously unsuspected bronchogenic tuberculosis. It is found as often above as below the clavicle, and appears as a group of small foci or as a non-homogeneous shadow as frequently as in the form of a homogeneous cotton-wool shadow (*Frühlinfiltrat*, or "early infiltration"). Help in deciding whether the lesion is active or not must often be obtained from serial radiographs.

Help in assessing the outlook for the lesion is obtained from serial radiographs and by finding the causative factor or factors; mode of origin, massive contact, and lowered resistance must be considered.

Treatment will depend to some extent on these factors. Treatment in the home may be considered under certain circumstances, but institutional treatment is usually essential.

Rest in bed until the lesion is quiescent is indicated whenever institutional treatment is advised. Collapse therapy should be used in addition when there is no evidence of regression of the lesions within a very few weeks. Reasons for these conclusions are discussed.

The relations of tubercle bacilli in the sputum to the definition of early bronchogenic tuberculosis and the classification of tuberculosis are discussed, as well as the significance of this finding in connexion with treatment.

The importance of mass radiological examinations in connexion with the detection of early bronchogenic tuberculosis is stressed, but the method to be used is critically examined. The conditions under which mass radiological examinations are likely to play a decisive part in the eradication of tuberculosis of human origin are brought forward.

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The papers by Hart, Hilton, and Morland deal with tuberculosis in medica students detected by radiological examination. The papers by Schemmel, by Uehlinger, and by Voigtmann deal with "round foci."

J. Fénéon (*Thèse de Paris*, 1940, No. 189) states that it has been well known since Fournier's time that syphilis may give rise to osteo-articular lesions. They are rare, however, and occur in the course of active syphilis. The part played by syphilis in the aetiology of chronic rheumatism is much more important, hydrarthroses and arthritis of the hip-joint being the most frequent manifestations. It is often difficult to determine the existence of syphilis in an old-standing case which has been inadequately treated and may be associated with other infections. Inconstant results are yielded by chemotherapy, which should be employed with caution as the patients are affected by diffuse sclerosis. Orthopaedic surgery is important in the correction of deformities.

EMPLOYMENT OF AIR-RAID NOISES IN PSYCHOTHERAPY

BY

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A large proportion of patients admitted to a neuropathic military hospital revealed that their neurotic breakdown was either determined or in part precipitated by the unaccustomed stress of noises, such as gun-fire, shell-bursts, exploding bombs, sirens, planes, and dive-bombing. Some of these soldiers were Dunkirk casualties, but the majority were men who had not served outside England. Experience showed that treatment along orthodox psychotherapeutic lines, which included physical training, occupational therapy, route marches, games, etc., was impeded in these cases by too quiet an environment in hospital. While other symptoms had been resolved there remained a certain hypersensitiveness to air-raid noises.

The type of patient who came into this group and who formed the material for the treatment here outlined consisted of those in whom anxiety was the main presenting symptom. Their symptoms were related closely to experiences of a traumatic nature—physical or psychological—when in the "front line." It was considered that a close approximation between hospital life and life in the Army was necessary if these men were to remain well when returned to their units. An attempt was made to "decondition" the state of hypersensitiveness to warfare sounds by reproducing the disturbing noises till the patients gradually became more normal in their reactions.

Method

At first the apparatus used for reproducing these noises was rather crude, consisting of a small portable field siren and an assortment of tin boxes and sticks. Later, with the helpful co-operation of the B.B.C., it was possible to make use of gramophone records of actual warfare. Technicians made to our specification records of sirens, the firing of A.A. and machine guns, sounds of planes, dive-bombing, and explosions. Individual sounds or a composite effect could be reproduced when required. Records combining reassurance talks with actual bombing noises were also made. The following technique was employed:

The patient was given a simple explanation of the treatment and its object. He was placed in a state of relaxation, and details of the pulse rate, respiration, blood pressure, presence of tremors, restlessness, and the like were recorded. He was then subjected to the particular sound deemed to be the precipitant in his case. Notes were made of changes occurring in the physical and mental state, and after a short rest period the stimulus was again given. Depending on the response obtained, this was repeated three to seven times at each session, at the end of which the mechanism and meaning of fear were explained. The record chart, revealing a gradual improvement in responses—a phenomenon almost invariably present—was shown to the patient after the first session.

Reassurance and encouragement on common-sense lines were given to certain patients. They were told: "Men, women, and children in our badly bombed cities have developed a new lease of life. They are in better mental trim than those in safe areas. They have faced the raids, have found them not so bad as anticipated, and have got over them. They carry on with their jobs

and take a pride in being fit for fire-fighting and other duties. You can do the same, and this treatment will help you to get accustomed to raid noises."

Conditioning and Abreaction

Though the procedure was intended to be a means of "conditioning" cases to noxious sounds, it soon became evident that it could be used as a speedy and practical method of abreacting patients. The process of letting a patient re-live terrifying emotional experiences has a therapeutic effect. As a measure for producing abreaction the employment of war noises is much simpler than hypnosis or hypnonarcosis. It is quick, effective, and does not demand too great technical skill. The patient is enabled to recall terrifying incidents which had determined his symptoms, and by expressing them in the secure atmosphere of the hospital his self-control and confidence are helped. The following case illustrates the use of the method as an abreactive agent.

A private aged 22 who was in good health until shelled badly in France developed acute anxiety symptoms, thereafter tending to become worse when in bombing raids in this country. After admission to hospital he was given a course of "sound-therapy," and on the first application he became very agitated, volunteering the information that the noise "brought it all back again." The blood pressure and pulse rate showed marked increase after hearing warfare noises. Though the patient was aware that the sounds were artificial, he reacted briskly when the stimulus was given, vivid memories of the initial traumatic experience being recalled.

It was established in a number of cases that this procedure could easily reveal a wealth of psychological material, and by releasing emotional tension have a beneficial effect.

Some people cannot stand up to the stress of noises without help. It is not a question of "scrimshanking" but of constitutional make-up. They can be helped by realizing that knowledge and a sense of security will see them through. Giving them sane simple explanation and advice and getting them accustomed to disturbing stimuli increases their stability and sense of security and relieves apprehension and exaggerated fears. Our experience would indicate that the repetition of noxious stimuli is of value in restoring function in these cases. The principle of conditioning is very much that of the horseman who mounts immediately after a fall in order to prevent the association of fear and riding.

One man who complained of trembling, palpitation, and loss of control during air raids since the Dunkirk evacuation was conditioned to warfare noises in a week, and during subsequent air-raid alerts was no longer disturbed, being finally discharged to duty. Another soldier, with a similar history, at first reacted so strongly to the sounds given that he rushed screaming from the room. At the end of six days' treatment he was perfectly calm and showed no reaction whatever.

Conclusion

Air attack is being employed on all fronts to demoralize our people. It is now evident, however, that the anticipated number of psychiatric casualties as a result of air raids has not been justified. Actually there has been no increase in the incidence of neurosis or psychosis in our bombed cities. A corporate sense of discipline, preparedness, and individual effort has maintained morale. Fear has to a large extent been dissipated by the activity of fire-fighting and other defence measures. Fear, which is simply a normal protective instinct, can be countered by enlightenment, and aerial bombardment is unlikely to achieve its demoralizing object if the experience is not a complete surprise. Apprehension and anxiety concerning air raids are more likely to affect those who are inactive and have not been accustomed to warfare noises. Repetition of bombardment noises would appear to assist in raising the power of endurance and in enabling the individual to stand up to this new form of attack.

Our thanks are due to various members of the B.B.C. staff for their valuable help in producing the records used in this investigation. We are also indebted to Colonel G. W. Will, O.B.E., for permission to investigate cases under his care.

CHEMOTHERAPY IN ACUTE MIDDLE-EAR DISEASE: "MASKED MASTOIDITIS"

BY

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I have recently had three cases (quoted in detail below) referred to me in quick succession which have much exercised my mind on the subject of chemotherapy in acute disease of the middle ear.

In view of Dr. J. B. Jessiman's (1941) article on the subject, which drew forth prompt criticism from Mr. Lionel Colledge (1941), it would seem that there is ample justification for uttering a warning against putting *too* great reliance on drugs of the sulphonamide group. They have admittedly proved of marked value in the control of infections of the middle-ear cleft, but it is a mistake—which may have tragic consequences—to assume that, quite irrespective of whether myringotomy has or has not been done, all is of necessity well with the patient because the temperature has fallen, mastoid tenderness has disappeared, and the other symptoms and signs have cleared up. Such cases, indeed, call for very careful watching, since the sulphonamides can "mask" a mastoiditis most effectively, while serious complications may develop in the most alarmingly sudden manner.

Furthermore, it should be noted that in each of the cases quoted below sulphapyridine has been employed. Now, this agent is excellent for pneumococcal infections, but even its most enthusiastic supporters must admit it to be of very considerably less value than sulphanilamide where the infection is of streptococcal origin. After all, pneumococci are, it is true, responsible for many cases of middle-ear infection, but a number of cases *are* undoubtedly due to streptococci or other organisms. We should therefore be on our guard against thinking as it were in terms of sulphapyridine to the exclusion of sulphanilamide. Such blind faith can only result in a proportion of failures, and these will inevitably bring quite unwarranted discredit on a group of most valuable therapeutic agents.

It is suggested that the correct procedure in every case of threatening or frankly developed middle-ear infection is to take swabbings from the tonsils, nasopharynx, and/or purulent discharge itself (whether the result of perforation or myringotomy) and, if bacteriological examination reveals the presence of streptococci, then sulphanilamide (and not sulphapyridine) should be administered. It is only by such conscientious use of the appropriate member of the group that we can secure more consistently satisfactory results and so gain for these agents that confidence in them which is their just due.

Lastly, while agreeing with most of the relevant comments by Mr. R. Thomas (1941), I cannot find myself in agreement with his expressed wish that "the day will soon come when this simple operation [he specifies "paracentesis"] will become part of the armamentarium of every general practitioner." In the first place, paracentesis has been rightly

displaced from favour by the far more effective procedure of myringotomy; and, secondly, "every general practitioner" does not possess the experience and nicety of judgment which alone can decide whether myringotomy still has a reasonable chance of averting an acute mastoid or whether things have already gone too far for anything short of immediate mastoidectomy to have a hope of relieving the condition and possibly preventing a catastrophe.

Case I

A gunner aged 22 was admitted to a military hospital on January 17, 1941, with a history of left otalgia followed by otorrhoea. Temperature 99.4°, pulse 80. "Exacerbation of an old C.O.M.S.(L)" was diagnosed. Next day temperature tended to swing between 100.6° and 97.4°. On the 19th it settled to normal, and he was given guttae glyc. and phenol, fomentations, s.v.r. drops, and mist. aspirin. He was discharged to a convalescent home on the 25th, with normal temperature but profuse otorrhoea. From January 28 to 31 sulphapyridine, 1 gramme four-hourly, was given. Temperature was very slightly irregular above and below normal. He was transferred to a convalescent depot on February 7.

On February 10, when referred to me, there was thin somewhat offensive left otorrhoea, slight deafness in the left ear, medium-sized postero-inferior perforation, but no vertigo or tinnitus. He was returned to the convalescent depot with the recommendation that he be kept under close observation and that dry mopping and insufflation of 1% iodoboric powder be carried out. On the 13th he was readmitted to hospital with general malaise and severe pain behind the left ear. Otorrhoea was profuse and the left ear was pushed somewhat forward; there was no mastoid tenderness, but the patient looked ill. Subacute left mastoiditis was diagnosed. The next day left epitympano-mastoidectomy was performed. Very extensive involvement of the mastoid region was found. The bone was of mixed cellular and sclerotic type. Aditus, attic, antrum, and cells contained pus under some pressure. Healing by first intention was secured, and recovery was uneventful; the otorrhoea soon dried up, and there was very little loss of hearing.

Case II

A lance-corporal aged 21 was referred to me at a military hospital on January 21, 1941, with a history of having first noticed left-sided otorrhoea while on leave. There was slight deafness, but no pain; trismus, said to date from the extraction of a left lower wisdom tooth, was present. He stated that he had been treated by a civilian doctor and given, among other things, tablets of sulphapyridine, but no details as to dosage, etc., were available. He looked ill. There was a moderate amount of thin non-offensive otorrhoea, left cervical adenitis, and medium-sized postero-inferior perforation, but no mastoid tenderness.

He was admitted and kept under close observation, with dry mopping of the otorrhoea, counter-irritation over the cervical glands, gargles, and mentholization. During the next few days the trismus improved, but the temperature showed a slight tendency to swing between 98° and 99°. In the afternoon of January 26 there was a sudden exacerbation, with malaise, swelling of the left parotid region, slight left facial paresis, and gradual filling up of a fluctuating swelling on the posterior aspect of the lobule of the left ear. On the 27th he had a definite toxic appearance; the above-mentioned swellings had increased and the left facial paresis had deepened. Temperature normal; pulse 98. Left epitympano-mastoidectomy was performed. There was generalized osteomyelitis in an acellular mastoid with a perforation near the tip, "tracking" into the lobule of the ear and into the parotid region. This was thoroughly cleared and the wound packed open, secondary suture being performed on February 5. The wound then healed by first intention, the facial paresis recovered completely, the otorrhoea dried up, and the perforation in the drum healed. The hearing is good.

Case III

A second-lieutenant aged 28 was admitted to a hospital on February 18, 1941, with severe otalgia in the left ear of sudden onset and a history of acute left otitis media two years previously. Slight pulsatile left otorrhoea was present, but no mastoid tenderness. Sulphapyridine and a spirit-and-flavine wick were used, and on March 11 he was given a week's sick leave, the ear being then dry and all symptoms relieved. On March 15 diplopia developed, and on the 18th he consulted the eye specialist, who referred him to me. He gave the following history: For some days he had had fairly severe neuralgic pain centred somewhat vaguely between the left ear and the left eye, which had gradually changed to a dull ache behind the left eye; then on the 15th, as stated above, he had for the first time noticed the diplopia. On examination I found complete paralysis of the left external rectus; in other words, he presented the complete picture of the Gradenigo symptom-complex, indicating the presence of petrositis. A small perforation was found in the anterior portion of Shrapnell's membrane, from which a thin trickle of pus was escaping. Radiographs showed considerable relative radio-opacity of the left mastoid region and the petrous pyramid, with loss of the cellular outlines.

A left Schwartze mastoidectomy was performed on March 21. There was widespread involvement of the mastoid cells, which contained pus, while the mucosa was thickened. Two polypi were impacted in the aditus, and on their removal pus under considerable pressure escaped from the attic region and the middle ear. Healing took place by first intention, and convalescence was uneventful. All symptoms have been removed, while with the assistance of electrical stimulation of the paralysed muscle complete recovery from the paralysis has been secured and the diplopia has disappeared. The perforation in the drum has healed and the hearing seems to be normal.

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Medical Memoranda

Intestinal Haemorrhage as a Complication of Sulphonamide Therapy

The recent occurrence of melaena in two children under treatment with sulphonamide drugs stimulated an inquiry into the recorded incidence of this complication. The scanty references in the literature and the absence of records of its occurrence in this country make these notes and observations of value.

Case Reports

Case 1.—A boy aged 5 was admitted to the Southport Infirmary on January 23, 1941, with a history of severe vomiting of two days' duration. Lumbar puncture produced 4 c.cm. of turbid fluid from which meningococci were later grown on culture. Next day he was given 0.5 gramme of sulphapyridine soluble intramuscularly and transferred to the borough isolation hospital. On admission he was drowsy and irritable, and the temperature was 98.4° F. He did not appear to be very ill. Soluseptasine 0.5 gramme intramuscularly was ordered four-hourly. Next day after five injections his temperature had remained normal, but head retraction and opisthotonos were pronounced. lumbar puncture produced no fluid, and cisternal puncture only 2 c.cm. of opalescent fluid. Sulphapyridine soluble 0.5 gramme intramuscularly was ordered three-hourly. On January 27 the boy was much improved and took 0.5 gramme of sulphapyridine by mouth four times daily for four days. On January 31 he appeared normal, and received three 0.5-gramme doses of sulphapyridine, and on February 1 two doses of 0.5 gramme each. In the night of February 1 he passed a small tarry motion, and on February 2 two large melaena stools. He was very pale, but his condition did not give rise to anxiety. Parenteral salines were given. As we were unable to account for the melaena a blood film was made late at night and suggested a diagnosis of myeloid leukaemia. The temperature was 99° F., the spleen was not palpable or enlarged to percussion, the liver was not enlarged, no enlarged glands could be felt, no petechiae were seen, the urine was normal, and there was no evidence of jaundice. The blood film, however, showed a considerable increase of white cells, estimated at more than 100,000, of which 92% were polymorphs, 6% myelocytes, and 2% lymphocytes. The red cells were rather pale, and showed anisocytosis; 2% nucleated red

cells were found. Unfortunately the cell counts were deferred until next day and the child collapsed and died suddenly during the night.

Case 2.—A girl aged 8 was admitted to the Southport Infirmary on February 12, 1941, with a history of headache and vomiting of a few hours' duration. Lumbar puncture produced 6 c.cm. of opalescent fluid from which meningococci were later grown on culture. The child was admitted to the borough isolation hospital the next day, after receiving an intramuscular injection of 1 gramme of sulphapyridine soluble and 1 gramme of sulphapyridine by mouth. On admission she was very listless and semi-comatose, temperature 100.4° F. Sulphathiazole 1.5 grammes was ordered four-hourly. The temperature became normal the next day and did not rise above 99° F. thereafter. On February 14, following difficulty in swallowing, 1 gramme of sulphapyridine soluble was given intramuscularly four-hourly, followed by sulphathiazole 0.75 gramme four-hourly for three days. On February 18 the child did not appear well and seemed more comatose. Seven grammes of sulphathiazole was given in the next twenty-four hours, when it was finally stopped. On February 20 she passed a small melaena stool, but remained well and did not complain. A blood film appeared normal and a white cell count totalled 14,200. On February 21 another final melaena stool was passed, and the child thereafter progressed satisfactorily until discharge on March 10.

DISCUSSION

In neither child was there a history of a tendency to bleed and the family history in each case was negative. In Case 1, apart from the abnormal findings in the blood film, there were no clinical signs to suggest that the child was suffering from myeloid leukaemia, but the melaena was originally attributed to this possibility in the absence of any more feasible explanation. The occurrence of melaena in Case 2 gave reason to the consideration that the bleeding in Case 1 had been due in large part at least to the sulphonamide drugs.

Long and his associates (1940) report the rare occurrence of hyperleucocytosis during sulphanilamide and sulphapyridine therapy, generally in the presence of acute haemolytic anaemia, of which there was no evidence in this case. They also report that unexplained bleeding from the gastro-intestinal tract has been seen in one or two cases of sulphanilamide and sulphapyridine therapy, and that one patient who received sulphapyridine had bleeding severe enough to cause death. They record no instance of gastro-intestinal bleeding following sulphathiazole. Blake recorded two instances of gross intestinal haemorrhage in patients receiving sulphanilamide, in neither of whom was there any other plausible explanation for the untoward reaction.

These two records of melaena occurring among a comparatively small number of patients receiving sulphonamide drugs may stimulate the interest of others with greater experience and better facilities for investigation and lead to a better knowledge of its true incidence.

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H. D. Wright (*J. Path. Bact.*, 1941, **52**, 237), in a record of the three types of *C. diphtheriae* in 8,040 cases of diphtheria in Liverpool during 1937-40, states that this period was marked by a notable increase in the number and proportion of *gravis* cases. There was a slight decrease in the proportion of cases in the age period 5-9 years. The difference in age incidence between the different types was slight. The case fatality was highest in the *intermedius* infections, particularly among the older children, and lowest in the *mitis* group. The greatest number of deaths were due to the *gravis* type. Deaths from toxaemia predominated in the *intermedius* and *gravis* infections and from pneumonia or respiratory involvement in the *mitis* infection.

Reviews

HARDY ANNUAL

The Medical Annual, 1941. A Year Book of Treatment and Practitioner's Index. Fifty-ninth year. Editors: H. Letheby Tidy, M.D., F.R.C.P., and A. Rendle Short, M.D., B.S., B.Sc., F.R.C.S. (Pp. 516; 39 plates, plain and coloured. 23s. net.) Bristol: John Wright and Sons, Ltd.; London: Simpkin Marshall, Ltd.

This valuable work, as its devotees know, is published by Messrs. John Wright at Bristol, a town that has borne the full brunt of enemy attacks from the air. The publishers and the editors have not, however, been deterred by what must have been considerable difficulties, and both are to be congratulated on maintaining the standard of the familiar green-covered volume. There is one small criticism that we would make. In a yearbook that is primarily meant for the general medical reader we doubt whether there is much point in including special plates illustrating, for example, the prevention of elephantiasis chirurgica, seminoma of the testis, an operation for persistent thyroglossal duct. The illustrations are, as usual, very well reproduced, and there are a number of excellent line drawings in the text.

It is impossible to refer in detail to the numerous items, arranged in encyclopaedic form from A to Z. The article on vaginal thrush is accompanied by two instructive half-tone illustrations; a long and helpful article on electro-encephalography is contributed by Mr. Grey Walter and Prof. F. L. Golla; the two editors—Dr. Letheby Tidy and Prof. Rendle Short—contribute articles on the medical and surgical aspects respectively of abdominal disorders; Prof. R. M. F. Picken describes schistosome dermatitis, which so far has been found to occur in one place only in Great Britain—Roath Lake, Cardiff. The common and the uncommon all receive skilful treatment at the hands of practised commentators.

STATISTICAL STUDIES OF TUBERCULOSIS

Studies on Tuberculosis. Four Papers by Different Authors. The American Journal of Hygiene Monographic Series, No. 16, 1941. Baltimore: The Johns Hopkins Press. 1941. Publication financed by the Rockefeller Foundation, New York City.

This monograph is devoted to four papers describing two series of epidemiological investigations.

Eugene L. Opie, Persis Putnam, and E. Joyce Saward portray the spread of tuberculosis in negro families of Jamaica, B.W.I. The disease follows a much more rapid course than in the white people of European extraction, and is readily transferred from the first sufferer in a family to other members of the household, adults as well as children, so that many of them may die within two years after the disease has been introduced into the family. The proportion of those with tubercle bacilli in the sputum is much greater than among white persons of the United States, and greater than among American negroes. This factor and uncleanly habits, unhygienic housing conditions, and lack of facilities for segregation all promote the spread of disease in Jamaica. Though the tuberculin reaction in Jamaica, as elsewhere, has little value as an index of manifest disease, the frequency of lesions visible radiographically and of manifest disease increases with intensity of reaction. From what has already been said, it may be anticipated that asymptomatic and latent lesions were found much less often in Jamaican negroes than in white adults (and even less frequently than in American negroes). The authors conclude that the high level and rising incidence (with age), frequency, and mortality from tuber-

culosis in the Jamaican adolescents and adults following exposure to the disease occur as the result of exogenous infection.

A. H. Graham, P. W. Auston, and Persis Putnam made a survey of tuberculous infection in a rural area of East Alabama, and traced the fate of persons exposed to tuberculosis in white and negro families. Manifest tuberculosis among negroes was found to begin earlier, run a shorter, sharper course, and more often end fatally than among white persons. These were characteristic differences, as was the higher frequency of latent tuberculosis among white persons—that is, among negroes lesions were more likely to progress to disease and death; among white persons there was more tendency toward healing and calcification. The authors do not doubt that tuberculosis spreads from persons suffering with the disease to those in contact with them; that this is true of persons whose exposure begins in adult life as well as those first exposed in infancy, childhood, or adolescence; and that exogenous infection occurs in rural as well as in urban areas.

These elaborate, carefully worked out statistical studies illustrate once more the importance of natural resistance in tuberculous infection, and the role of exogenous infection in the incidence of manifest tuberculous disease at all ages in people with low natural resistance. In our opinion it would, on the other hand, be unwise to assume that the latter holds good to an equal degree in regard to pulmonary tuberculosis in adults among the more resistant European communities.

PRACTICAL ORTHOPAEDICS

Orthopedic Surgery for Nurses, including Nursing Care. By Philip Lewin, M.D., F.A.C.S. Third edition, revised and reset. (Pp. 462; illustrated. 17s. 6d. net.) Philadelphia and London: W. B. Saunders Company. 1941.

Orthopaedics is a specialized branch of surgery, but its principles can never be divorced from those of general surgery. In this country nurses usually receive their orthopaedic training before their general training, and in consequence the teacher of orthopaedics labours under the disadvantage of having students with little or no knowledge of pathology and general surgical principles. It is essential that the student-nurse should build her storehouse of knowledge not on the shifting sands of current orthopaedic practice but on the rock of general surgical principles. The ideal textbook must first discuss the anatomy, physiology, and pathology of the framework of the body, and the principles of the surgery of wounds, infections, and deformities must be clearly enunciated. This textbook fails singularly in this respect, and is concerned rather with the accumulation and tabulation of a vast amount of detail more suitable for a medical graduate. For instance, should any student-nurse be expected to know the thirty-seven differential diagnoses for tuberculous disease of the spine as listed on p. 150? Again, in the chapter on the orthopaedic operating room, though the author sets out in detail many aspects of theatre routine, he does not mention the reasons for and principles of asepsis. Further, in the chapter on fractures, one of the least commendable in the book, the three cardinal principles of treatment are obscure, and there is practically no mention of compound fractures. However, such criticism may be unjust, since the book is primarily intended for American use, where the nurse may already have been well grounded in general surgery.

For a graduate-nurse or medical student this book has a great deal to commend it. Its chapters are well arranged and the material is up to date, even such matters as arthrograms for congenital dislocation of the hip and plasma transfusion for shock being mentioned. The book contains a wealth of practical detail, particularly in the chapter on orthopaedic nursing care. The chapters on poliomyelitis are excellent and deal with the subject more thoroughly than any English textbook, and here the principles of treatment are clearly explained.

This book of almost 450 pages covers the whole field of practical orthopaedics and includes over 200 well reproduced diagrams and illustrations.

PSYCHOLOGY OF BREAST-FEEDING

The Nursing Couple. By Merrell P. Middlemore, M.D. With an introduction by Edward Glover, M.D. (Pp. 195. 7s. 6d.) London: Hamish Hamilton Medical Books. 1941.

When psychologists make assertions about infant feeding, paediatricians and obstetricians are apt to feel that enthusiasm is proving more of a stimulus than experience. For this reason the late Dr. Merrell P. Middlemore's book on *The Nursing Couple* is of great value, for here is a medical practitioner, trained as an obstetrician and as a psychologist, recording her observations and conclusions as a result of studying the behaviour of newborn babies at the breast in a hospital ward, and hence, possibly for the first time, it is likely that some of the truth on this important subject has been set down with scientific accuracy. That psychological factors enter into breast-feeding, successful and unsuccessful, is well recognized, but Dr. Middlemore's painstaking analysis sets out in some detail what these factors actually consist of, and all concerned with breast-feeding will learn much from a close study of the book. It clearly emerges that the nurse is the dominating figure in the successful establishment of lactation. Too stern a technique, too rigid a programme, and a lack of sympathetic understanding of the emotional background of the nursing couple—mother and baby—spell failure. It is equally clear that some sort of programme is necessary, and it is enthusiasm rather than experience that has led Dr. Edward Glover in his introduction to suggest that all will be well if babies are fed when they are hungry. It is just such lack of "discipline" that led the late Sir Frederick Truby King to initiate his great work—for as superintendent of a mental home he saw the wrecks produced by the absence of some sort of order in the nursery. Dr. Middlemore's book should certainly be read by all doctors and midwives, and much of its contents will help the expectant mother.

Notes on Books

Control of Pain in Dental Practice, edited by Dr. J. L. T. APPLETON (Lippincott, 15s.) contains a series of articles by different contributors which deal with the innervation of the teeth, local anaesthesia and general anaesthesia. The contributors are members of the medical and dental schools of the University of Pennsylvania. An article by Dr. H. Prinz on the early history of pain control in dentistry is of special interest because the medical profession owes to the dental profession the discovery of the use of nitrous oxide and ether as anaesthetics. In a chapter on the pharmacology of drugs, Prof. C. F. Schmidt gives an interesting summary of the advantages and disadvantages of intravenous anaesthesia.

Medical Organization and Surgical Practice in Air Raids (J. and A. Churchill, 12s. 6d.) first appeared in March, 1939. It has since been reprinted twice, and the authors, Brigadiers P. H. MITCHINER and E. M. COWELL, have now brought out a second edition. Between the two editions the war has happened, and the first two chapters, both dealing with air raids, have consequently been rewritten in the light of bitter experience. Other chapters have also been revised to include, for example, further information on the sulphonamides and the use of blood plasma. Mitchiner and Cowell are sure guides to the many problems embraced by the title of their book, and the second edition deserves the success that attended the publication of the first.

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EQUINE ENCEPHALOMYELITIS

It is becoming only too obvious that in order to unravel the many problems associated with virus diseases one must be, among other things, a highly competent field naturalist. African horse sickness, for instance, can remain latent in an area for many years in the absence of all Equidae, though how or where it remains latent is unknown. Yellow fever, it seems, can somehow maintain itself in the absence of all human beings; infection of man is, in fact, merely an unfortunate incident in the life history of a virus that primarily exists as an inapparent infection of animals. There are much the same lacunae in our knowledge of what has been called, somewhat unfortunately, "equine encephalomyelitis." For some years past a very fatal encephalomyelitis of horses has been recognized in the New World, from Canada to the Argentine. Cases are seen chiefly in the late summer and autumn, and in some years enormous epizootics occur: in 1938 in Minnesota alone there were 23,686 cases in horses, with 4,979 deaths. The problem of equine encephalomyelitis was complicated at the outset by the discovery made by Ten Broeck and Merrill[1] that there exist in the U.S.A. two strains of the virus which are immunologically quite distinct. These two strains are known as the eastern type and western type respectively, the Appalachian Mountains forming a rough dividing line. The symptoms and the pathological changes caused by the two viruses are, however, closely similar both in horses and in experimental animals, except that the disease is more fulminating when caused by the eastern strain. Both viruses are of the same size as determined by differential filtration and centrifugation, while both are quite distinct from the causal agent of European equine encephalomyelitis, Borna disease, as well as from the virus of a Russian form of equine encephalomyelitis, which is most probably an atypical rabies. An Argentine strain, however, was identical with the Western American virus; but a Venezuelan strain, on the other hand, examined by Beck and Wyckoff,[2] was immunologically different from both American strains, though perhaps remotely related to the eastern virus. Thus at least three distinct immunological strains of the equine encephalomyelitis virus exist in the New World. Now, as is well known, after exhibiting a long geological succession all Equidae suddenly died out in America at the end of the Pleistocene Period. They were not reintroduced until the time of the Spanish conquest. The question therefore arises whether the various strains of equine encephalomyelitis virus have arisen since the discovery of the New World by Columbus, or whether they have lived in other hosts, causing inapparent infections. The first step in the elucidation of this problem was the discovery that both the eastern and the western viruses could be transmitted by mosquitoes under laboratory conditions. While the eastern strain is transmitted by *Aëdes cantator*, a salt-marsh mosquito, the western variety is transmitted by *A. aegypti*, *A. vexans*, *A. atropalpus*, *A. triseriatus*, *A. nigromaculis*, *A. taeniorhynchus*, and *A. albopictus*. *A. sollicitans* transmits both strains.

Although equine encephalomyelitis tends to occur in the late summer and autumn, no mosquito has actually been found infected under natural conditions, the same being true also of *Dermacentor andersoni*, a tick which Syverton and Berry[3] have found capable of transmitting the western strain of the virus. A fresh complication arose when it was found that both the eastern and the western strains were causing a highly fatal encephalomyelitis in man in some outbreaks, as in Saskatchewan in 1938 in the absence of mosquitoes. The first case was described as long ago as 1930 by Meyer, Haring, and Howitt,[4] but it was only in 1938 that it became evident (cf. Fothergill *et al.*,[5] Feemster,[6] Webster and Wright,[7] and Howitt[8]) that a very considerable number of infections were occurring throughout the United States, more especially in children. Many of these were fatal, but Farber and his colleagues,[9] Davis,[10] and Platou[11] have more recently described cases with residual paralyses, mental changes, and other nervous sequelae. Shortly after human cases had been described in the New England States, Tyzzer, Sellards, and Bennett,[12] and later Van Roekel and Clark,[13] and Beaudette[14] all isolated the eastern virus from wild ring-necked pheasants, while Fothergill and Dingle[15] obtained the same virus from wild pigeons. Whether pheasants and pigeons form the only reservoir from which horses and men can be infected remains uncertain. Under laboratory conditions a very considerable number of wild birds and rodents such as voles, rats, and mice can be readily infected, while many wild and domesticated birds either succumb or carry the virus in their blood even though they fail to show clinical symptoms (cf. Davis[16] and Howitt[17]).

It is obvious that transmission of the infection, possibly by mosquitoes, to horses and man represents but a part of the story: the lacunae can be filled in only by intensive oecological studies. So far observations have yielded largely negative results; Howitt,[17] for instance, in California failed to isolate the virus from the brains of forty-three wild animals and birds, representing fourteen different species. Davis,[16] however, brought forward evidence that birds such as the domestic sparrow, pigeon, and cow-bird can acquire the virus by the bite of infected mosquitoes, and that infected birds may serve as a source from which mosquitoes can become infected. C. Ten

[1] *Proc. Soc. exp. Biol.*, N.Y., 1933 **31**, 217.
[2] *Science*, 1938, **88**, 530.
[3] *Science*, 1936, **84**, 186.
[4] Ibid., 1931, **74**, 227.
[5] *New Engl. J. Med.*, 1938, **219**, 411.
[6] *Amer. J. publ. Health*, 1938, **28**, 1403.
[7] *Science*, 1938, **88**, 305.
[8] Ibid., 1938, **88**, 455; 1939, **89**, 541.
[9] *J. Amer. med. Ass.*, 1940, **114**, 1725.
[10] *J. Pediat.*, 1940, **16**, 591.
[11] *Amer. J. Dis. Child.*, 1940, **60**, 1155.
[12] *Science*, 1938, **88**, 505.
[13] *J. Amer. vet. med. Ass.*, 1939, **94**, 466.
[14] *Proc. 3rd internat. Congress Microbiol.*, 1939, p. 303
[15] *Science*, 1938, **88**, 549.
[16] *Amer. J. Hyg.*, 1940, **32**, Section C, 45.
[17] *J. inf. Dis.*, 1940, **67**, 177.

Broeck,[18] it is interesting to note, found neutralizing antibodies in the sera of fowls from farms where horses had died from encephalomyelitis. There is thus suggestive evidence that birds may possibly serve in nature as alternative hosts for the virus of equine encephalomyelitis. Mammals may also play a similar part. Syverton and Berry,[19] in 1936, found that Richardson's ground squirrel, *Citellus richardsoni,* was highly susceptible to the western strain of the virus of equine encephalomyelitis, while one specimen was refractory to inoculation and presumably immune. In 1940 Gwatkin and Moore[20] showed that the brains of certain of these ground squirrels from Alberta harboured the virus. No virus was, however, found by Gwatkin[21] in some hundreds of ticks, *Dermacentor andersoni,* but Kitselman and Grundman[22] have recently reported isolating the virus in Kansas from assassin bugs, *Triatoma sanguisuga.* Thus by studies in various parts of America the full story of the equine encephalomyelitis virus is being gradually revealed.

EFFECT OF CARBOHYDRATE ON PROTEIN METABOLISM

It is seldom that experiments in metabolism are performed first on human beings and later on animals. This, however, has been done by Cuthbertson and Munro[23 25 27] in their investigation of the influence of carbohydrate eaten at the same time as protein or at a different time. Early observations showed that when carbohydrate is eaten at the same time as protein, and the calorie content of the diet is in excess of energy requirements, there is storage of nitrogen and sulphur, more especially when the excess calories are in the form of carbohydrate rather than of fat. Larson and Chaikoff,[24] working on dogs, found that to get this effect the carbohydrate must be taken less than four hours before or after the protein meal. Cuthbertson and Munro,[25] continuing their observation on human beings, found that a negative nitrogen balance of some 2 grammes daily was produced by eating the carbohydrate and protein moieties of an adequate diet separately over short periods of time. The nitrogen was lost mainly in the form of urea and was equally distributed between the day and night portions of the urine. If a part only of the dietary protein was dissociated from the carbohydrates the nitrogen balance was undisturbed. If carbohydrate in excess of energy requirements was ingested over long periods, storage of nitrogen and sulphur resulted whether the carbohydrate was taken with or separately from the protein.

Krebs[26] has observed that deamination by liver slices is inhibited in the presence of easily oxidizable substances such as lactic, succinic, and α-keto acids (but not glucose), and Cuthbertson and Munro suggest that when carbohydrate is ingested with protein it may yield a more active form of glucose within the body, and thus ensure that some of the amino-acids escape deamination and go to replace the effete products of endogenous metabolism. Thus nitrogen balance is attained. A surfeit of carbohydrate may save even more amino-acids from the deaminases, with the result that the storage depots are further charged with protein. More prolonged surfeit feeding of carbohydrate seems to result in a storage of carbohydrate also. Nitrogen balance on an ordinary diet in which the proportions of carbohydrate and protein vary is probably attained through the mechanism of storage and depletion of carbohydrate stores as needed. If all the protein is ingested separately from the carbohydrate, the deaminases are free to break down the amino-acids, and the excreted nitrogen consists of that taken in as protein plus the daily endogenous nitrogen.

To gain more exact information Cuthbertson and Munro[27] have experimented on rats. They fed four adult male rats, each of about 300 grammes in weight, on a diet of dried egg yolk (12%), dried egg albumen (6%), uncooked potato starch (17%), uncooked rice starch (40%), cane sugar (10%), butter (10%), De Loureiro's salt mixture (1931) (5%), Brewer's yeast extract 2 c.cm. daily per rat, and cod-liver oil two drops per rat per day. The mean daily intake per rat for seven days was 17.5 grammes. During the next twelve days the diet was separated into two fractions: fraction A consisted of the potato starch, rice starch, cane sugar, cod-liver oil, yeast extract, and half the butter and salt mixture; fraction B consisted of dried egg yolk, dried egg albumen, and half the butter and salt mixture. The A fraction (carbohydrate plus fat) was given freely at 8.30 a.m. each morning and the residue removed and weighed at noon. Of the B fraction (protein plus fat) 4.0 grammes were given to each animal at 4.30 p.m. each day, and the meal was always eaten within a few hours. After the first five days of this diet the rats were weighed fasting. During the next seven days they lost weight (average 7.0 grammes per rat), and their output of urinary nitrogen was 0.165 gramme. They were then given the A and B fractions mixed in amounts equal to the mean value of the daily intakes in the previous period. There was an average gain in weight of 5 grammes, and the daily output of urinary nitrogen fell to 0.145 gramme (with a mean difference from the average of 0.02 gramme). The experiment was then repeated on young rats (weighing about 66 grammes). They were first fed on a diet similar to that already described, and then one in which the protein part consisted of ashless casein (12 parts) and dried egg albumen (6 parts) only, the whole of the fat (as lard) and salt mixture being incorporated in the carbohydrate part of the diet. The "paired feeding" technique was followed—that is, each rat in the group receiving the two parts of the diet mixed together was given an amount equal to that which its "opposite" had eaten the previous day. This was particularly important, for the rats receiving the portions separately lost appetite for the carbohydrate fraction though not for the protein.

In both experiments there was practically no difference between the average increases in weight of the two groups of rats, though these were below the increase

[18] *Arch. Path.*, 1938, **25**, 759.
[19] *Proc. Soc. exp. Biol.*, N.Y., 1936, **34**, 822.
[20] *Canad. J. comp. Med.*, 1940, **4**, 78.
[21] Ibid., 1941, **5**, 113.
[22] *State College Agr. exp. Stn. tech. Bull.*, 1940, No. 50 (October).
[23] *Biochem. J.*, 1937, **31**, 694.
[24] *J. Nutrit.*, 1937, **13**, 287.
[25] *Biochem. J.*, 1939, **33**, 128.
[26] Ibid., 1935, **29**, 1620.
[27] *Biochem. J.*, **34**, 1002.

in weight of a group in the second experiment given an unrestricted mixed diet. In the second experiment, where nitrogen output was measured, the rats receiving the food fractions separately lost 0.0928 gramme of nitrogen, and those receiving the mixed fractions lost 0.0930 gramme. Thus the metabolism of protein in the young rat apparently remains unaffected by separating the protein from the carbohydrate moiety of the diet. It does, however, reduce the appetite, which is reflected in a small increase in body weight. The behaviour of the adult rat corresponds with that of the adult human being—namely, when protein and carbohydrate are eaten separately there is a small loss of nitrogen and also of body weight.

X-RAY INJURY AGAIN

Although the harmful effects of *x* rays on living tissues were noted within a few months of Röntgen's "preliminary communication," it was not until about 1903 that some consideration was given to the dangers to which those working with *x* rays might be exposed. Protective clothing and other devices made their appearance, but there were no satisfactory means of judging their efficacy. The first organized move towards protection against *x*-ray injuries was made by the British Röntgen Society in 1915, but the medical conscience was not generally aroused until a number of deaths occurred from aplastic anaemia in 1920 and 1921. In the latter year the British *X*-ray Protection Committee published the first set of protective recommendations; it stressed the importance of protection at the first International Congress of Radiology held in London in 1925, and three years later persuaded the second Congress to form an International *X*-ray and Radium Protection Commission, which subsequently adopted the British recommendations almost verbatim. It speaks well for the foresight of the British committee that the recommendations remained virtually unchanged by the revision made at the fifth International Congress, held in Chicago in 1937, but it is a poor reward for their labours that it should now be found necessary to publish the letter on page 175. There were not lacking signs even before the war that the medical conscience had gone to sleep again, a lapse due in part to the skill of the engineer in producing fool-proof apparatus. But even fool-proof machines are not meant to be used by fools. For example, the portable *x*-ray apparatus commonly supplied to E.M.S. hospitals gives an *x*-ray intensity of 165 *r*/min. at 15 cm. when running at 65 kV and 5 mA, so the radiologist gives instructions that the apparatus is not to be used without a 15-cm. cone. A surgeon in the theatre, however, asks the radiographer to remove the cone so that he can have the tube close underneath the patient; the intensity at 6 cm. distance is then 1,000 *r*/min., so that in one minute's screening he may not only burn the skin of the patient but almost sterilize his assistants as well. Because it is difficult for a radiographer working in the operating theatre not to obey the surgeon's orders, the responsibility of the surgeon for knowing what his order entails is all the greater. It is not impossible that some of the skin troubles put down to "plaster idiosyncrasy" are in fact due to excessive *x*-ray exposure, and for prolonged fluoroscopic work an accumulative timing device which turns off the apparatus when the total exposure reaches a certain previously determined limit is very desirable.

A related difficulty is occurring in radiotherapy, and is also probably due to the dispersal of hospital staffs over the countryside. Postal directions for the use of radium or radon in a patient whom the sender has never seen are at their best unlikely to serve the true interests of the patient, and at their worst are improper. It would be idle to deny that some of these difficulties have their origin in a feeling that radiologists are trying to maintain a kind of vested interest; but[1] "the first consideration is that the use of *x* rays and radium is dangerous both to the patient and to the doctor unless the latter thoroughly understands their use."

INHERITANCE OF HARELIP AND CLEFT PALATE

The problem of the inheritance of harelip and cleft palate is a difficult one, and no uncomplicated Mendelian scheme will fit the facts. Transmission is in general recessive, but the proportion of individuals affected is much less than the expected quarter. Furthermore, there is a sex difference, the condition being commoner in males than females. As in other similar instances, a two-gene hypothesis has been advanced: the combined action of an autosomal and a sex-linked gene, both recessive. Csik and Mather[2] have shown that the sex difference cannot be due to sex-linkage. It is fairly clear that only a proportion of the bearers of the abnormal gene show any malformation, and that, for some reason at present unknown, that proportion is higher in males. Mather and Philip, in an analysis in a recent paper,[3] use the methods associated with the names of Fisher and of Haldane, applying them to two large collections of data, those of Sanders and of Schröder. To add to the difficulty of analysis and interpretation Schröder's data were admittedly selected for high incidence. First of all it was found that the two sets of data differ. Sanders's data are homogeneous and indicate the presence of an autosomal recessive gene. Actually, it is possible that any one of several genes might be responsible; the methods used could not elucidate this point. Schröder's data are not homogeneous. While a proportion of cases is due to an ordinary recessive gene (or one of a number of such genes) others give clear evidence of partial sex-linkage. It is remarkable that almost simultaneously with Haldane's demonstration of partial sex-linkage in the transmission of spastic paraplegia[4] another instance should have been discovered. (Briefly, partial sex-linkage means the transmission of a gene situated on the pairing portions of the X- and Y-chromosomes and showing a far more subtle relation to sex than ordinary, sex-linked, X-borne genes, such as that responsible for haemophilia.) Having established that at least two genes must be responsible in Schröder's cases, a re-examination of the descriptions of the cases revealed that the genetic difference did correspond to a clinical difference, though not an absolute one, for the partially sex-linked cases tended to be more severe. The authors of this paper have performed a service in showing that, provided the new methods are used, successful analyses can be made when the genetic situation is far from simple, and, furthermore, when the data are far from perfect. The devising of the new methods has been a triumph of statistical skill, though fortunately their use does not demand corresponding mathematical abilities. Further examples of the proper use of the Fisher methods will be very welcome, however, to those who are not mathematicians and are starting to use them with some natural timidity.

[1] Wood, F. Carter, *J. Amer. med. Ass.*, 1931, **96**, 1760.
[2] *Ann. Eugenics*, 1938, **8**, 126.
[3] Ibid., 1940, **10**, 403.
[4] *J. Genetics*, 1941, **41**, 141.

LIVER FUNCTION IN GRAVES'S DISEASE

It has been shown by Elmer and his co-workers[1] that the liver is the organ most concerned with the excretion and detoxication of thyroxine. Liver damage in hyperthyroidism might, therefore, be of great clinical interest, and there is now evidence that it often occurs. This evidence, which has been reviewed by Lichtman,[2] who also contributes new data on cincophen oxidation and galactose tolerance, is derived from three sources. The administration of thyroxine to animals produces functional and anatomical changes in the liver; necropsy material from thyrotoxic patients has disclosed a high proportion of abnormal livers; and liver-function tests have frequently given abnormal results. One of the few uncertain links in this chain concerns the possible role of increased intestinal absorption in those tests of hepatic function which depend upon the oral administration of the test substance, and we have already noted in these columns[3] the divergent views of Althausen, Lockart, and Soley[4] and of Maclagan and Rundle[5] on the impaired galactose tolerance, which is evidently a characteristic finding. It appears that increased absorption occurs in thyroxinized rats and probably in thyrotoxic patients,[4] but it has not been shown that such increased absorption would necessarily impair galactose tolerance by itself, for it has not been studied apart from thyroid intoxication. The question is difficult to investigate directly in the human being, but it is significant that many of the intravenous liver-function tests, which must be independent of the absorption factor, have given positive results. Thus, Youmans and Warfield[6] found retention of phenoltetrachlorphthalein in the blood in twenty-two out of forty-eight cases, and Maddock, Coller, and Pederson[7] retention of bromsulphalein in eight out of thirteen cases. There was a positive Takata-Ara reaction in six out of fourteen of Ragins's cases,[8] while Haines, Magath, and Power[9] obtained abnormal results with the intravenous hippuric acid test in four of the six cases in which the test was done. It is still possible that increased absorption is partly responsible for the results where oral methods are used; if so, these might well possess an advantage from the purely diagnostic point of view. At present there is no general agreement on the clinical value of these tests in Graves's disease. Several authors have been impressed with the diagnostic possibilities and with the likelihood of relation between liver damage and thyroid crisis.[4 5] The latter is, however, denied by others,[7 9] and further work will evidently be necessary.

ISINGLASS AS A TRANSFUSION FLUID

In order to restore and maintain the volume of circulating fluid a transfusion fluid must answer the following requirements: (1) The molecule of the dissolved substance must be of such a size that the fluid will not leave the vessels too freely. (2) The solution must exert an osmotic pressure and possess a viscosity approaching as closely as possible that of whole blood. (3) It should be as nearly as possible isotonic with the contents of the red cells. (4) It must be non-antigenic and innocuous. A 7% solution of ordinary gelatin made from animal sources in 0.9% saline is satisfactory except as regards the last point. Cases have been recorded in which gelatin has been responsible for infection with anthrax or tetanus. Fish gelatin or isinglass should theoretically be free from such contaminations. N. B. Taylor and E. T. Waters[1] have just published some interesting experimental observations on the use of special purified isinglass in dogs after severe haemorrhage. A 7% solution in 0.9% saline was employed. This was found not to gel at room temperature. When the blood pressure had fallen to a dangerously low level after bleeding the isinglass solution was transfused slowly (in from 15 to 20 minutes) into the femoral vein. In most of the experiments haematocrit determinations were made before and after bleeding in order to check the proportion of the blood volume which according to calculation had been lost, though the authors realize that such figures are not altogether reliable. In experiments in which large quantities of blood were rapidly removed it was found that transfusion with isinglass, even when incomplete replacement was affected, caused and maintained a satisfactory rise in blood pressure, though the animals subsequently died, probably from other contributory factors such as unsatisfactory anaesthesia. In a series of survival experiments in which an amount of blood was withdrawn which might be expected to cause death in an untreated animal, very good results were obtained with transfusions of isinglass. The animals made complete and uneventful recoveries. It was found that a mild degree of sensitization which lasted only two weeks followed the transfusion. It is hoped that further purification may prevent such sensitization from occurring. The fate of isinglass after its introduction into the body is now being investigated. The authors suggest that it is probably broken down and used by the tissues, and is therefore preferable to gum acacia, which the body is unable to metabolize as a transfusion fluid. The viscosity of isinglass is about double that of serum and plasma; this, it is suggested, is also an advantage. It would appear from these preliminary studies that if a really pure non-sensitizing isinglass can be prepared it will merit more extensive trial on human as well as on animal subjects.

VITAMIN B_6 (ADERMIN)

Rat acrodynia, caused by a deficiency of vitamin B_6 in the diet, is characterized by symmetrical dermatitis with oedema and scaliness, mainly on the peripheral parts of the body—e.g., mouth, nose, paws, ears, and tail. Chick *et al.*[2 3] have distinguished three different types of skin lesions in rats cured respectively by riboflavin, filtrate fraction, and eluate fraction (containing vitamin B_6) from yeast extracts. During a deficiency of riboflavin, rats developed an eczematous condition of the skin, particularly of the nostrils and eyes. When deprived of the filtrate fraction, which contains pantothenic acid and probably other essentials also, the rats' coats were poor and matted and the pigmented areas over the heads and shoulders often became grey. The fur of the forearms and abdomen was frequently stained with a reddish exudate containing protoporphyrin. Rats deprived of the yeast eluate fraction (containing adermin) developed the characteristic dermatitis and, in time, a tendency to fits of an epileptic nature. These fits showed different stages—a sudden rushing about and leaping into the air, with the eyes protruding and sometimes suffused with blood; a helpless condition with muscular twitching of the limbs and tonic spasms; a comatose state with a slowed and weakened heart-beat and absence of corneal reflex; and gradual recovery, first of the head and fore-

[1] *Iodine Metabolism and Thyroid Function.* Oxford, 1938.
[2] *Ann. intern. Med.*, 1941, **14**, 1199.
[3] *British Medical Journal*, 1941, **1**, 367.
[4] *Amer. J. med. Sci.*, 1940, **199**, 342.
[5] *Quart. J. Med.*, 1940, **9**, 215.
[6] *Arch. intern. Med.*, 1926, **37**, 1.
[7] *West. J. Surg.*, 1936, **44**, 513.
[8] *J. Lab. clin. Med.*, 1935, **20**, 902.
[9] *Ann. intern. Med.*, 1941, **14**, 1225

[1] *Canad. med. Ass. J.*, 1941, **44**, 547.
[2] *Biochem. J.*, 1940, **34**, 580.
[3] Ibid., 595.

paws and later of the hind legs. Pure vitamin B_6 cured these rats and also prevented the onset of the condition in the control animals. Schneider *et al.*[4] have found that acrodynia may be cured by giving vitamin B_6 together with unsaturated fatty acids or the filtrate from rice bran extracts similar to the liver and yeast filtrate fractions. Apparently acrodynia in their rats was not the simple dermatitis due to a deficiency of vitamin B_6 only, but a more complicated one due to a deficiency of at least two factors. György and Eckardt[5] distinguished three different kinds of cutaneous lesions in rats which were supplied with vitamin B_6, aneurin, and riboflavin, and they also concluded that the rat needs at least one other member of the vitamin B complex for perfect nutrition. The use of vitamin B_6 in human nutrition has recently been reported by Spies *et al.*,[6] who obtained dramatic relief of symptoms (extreme nervousness, insomnia, irritability, abdominal pain, weakness, and difficulty in walking) in patients who had been treated successfully for pellagra and beriberi but had remained on their deficient diets and retained the above symptoms. Antopol and Schotland[7] obtained considerable improvement in the condition of 6 cases of pseudohypertrophic muscular dystrophy. It is, however, possible to give too much vitamin B_6. Unna[8] has found that the L.D.50 of vitamin B_6 hydrochloride for rats is 3.7 grammes per kilogramme following subcutaneous injection and 5.5 grammes per kilogramme following oral administration. Doses above 1 gramme per kilo produced toxic manifestations in dogs, rabbits, and rats, characterized by impairment of the co-ordination and tonic convulsions, but this dose was at least 1,000 times the therapeutic dose. The metabolism, circulatory and respiratory systems, and isolated smooth muscle organs of normal animals were not affected.

[4] *J. biol. Chem.*, 1940, **132**, 539.
[5] *Biochem. J.*, 1940, **34**, 1143.
[6] *J. Amer. med. Ass.*, 1939, **112**, 2414.
[7] Ibid., 1940, **114**, 1058.
[8] *J. Pharm. exp. Ther.*, 1940, **70**, 400.
[9] *J. Obstet. Gynaec. Brit. Emp.*, 1941, **48**, 1.

THE MENOPAUSE

Puberty and romance are not strangers. The young woman becomes conscious of new hopes and new powers which are undismayed by the occasional faint whisperings of a nameless fear. Autumn irrevocably follows summer, and so the years of full glandular activity and co-ordination lead at last to that stage of hormone readjustment which marks the critical period of "the change of life." Fears now predominate, for a while at least, though time often proves them ill founded when, instead of a dreaded disintegration, there is revealed that new physical and spiritual beauty which Whistler has immortalized in the portrait of his mother. From earliest times the menopause has been regarded as the critical stage in a woman's life, but it is surprising what confusion still exists in the minds of both laity and profession as to which symptoms are to be regarded as normal and which are warnings of impending or present dangers. There has been controversy for many years over the question whether an artificially induced causes more distress than a spontaneous menopause and whether symptoms are worse after irradiation or surgery. Hugh McLaren[9] has published two interesting papers on this subject from the department of obstetrics and gynaecology of Aberdeen University. His first dealt with the normal and the second with the induced menopause. In the first group it was found that hot flushes occurred in approximately 50% of cases before the menopause, but less commonly afterwards. They did not usually cause inconvenience, but the incidence of severe flushing was greater after than before. Post-menopausal atrophy of the genitalia was found to be by no means a constant feature, but when it did occur the vagina was involved at an earlier stage than the external genitalia. In over half the cases studied, however, there was little anatomical or physiological change. When the menopause was induced by irradiation or by removal of the ovaries it was found that hot flushes caused inconvenience in half the cases, being much more common than during a normal menopause. They seldom appeared, however, when a hysterectomy was performed with conservation of the ovaries. In view of the argument which has centred from time to time on this question of ovarian conservation these results are significant.

The analysis also revealed that atrophy of the vaginal mucosa was rare when ovarian tissue was conserved, but took place in 14% of cases of radiation menopause and in 28% when oophorectomy was performed with hysterectomy. A complication of radium therapy to which the author draws attention is the occurrence of vaginal strictures, which happened in 8% of his series. This figure excluded the many cases of stenosis of the vaginal fornices, which is common even after a normal menopause. The change thus induced in the anatomy and physiology of the vagina may have serious results in the domestic life of the patient, and the possibility of this should be remembered when the choice of treatment is being considered. Though there is much that commends radiation as a means of inducing the menopause, the superficial advantages must not be allowed to mask the real dangers. The greatest of these lies in the failure to select the suitable case carefully. In view of the possibility of overlooking an early carcinoma it can scarcely be over-emphasized that no woman should have a radiation menopause induced either by radium or by *x* rays before an exploratory curettage has been performed. It should also be remembered that excessive bleeding and intermenstrual bleeding are pathological, and without investigation should never be dismissed lightly as signs of "the change of life." The fact that such avoidable mistakes are still made is one reason why the menopause continues to be a critical period in the life of a woman.

THE HALF-YEARLY INDEXES

The usual half-yearly indexes to the *Journal* and to the *Supplement* will soon be ready. They will, however, not be issued with all copies of the *Journal*, but only to those readers who ask for them. Any member or subscriber who wishes to have one or both of the indexes can obtain what he wants, post free, by sending a postcard notifying his desire to the Accountant, British Medical Association House, Tavistock Square, W.C.1. Those wishing to receive the indexes regularly as published should intimate this.

In the *Supplement* this week (p. 15) we publish a letter which has been sent by the Secretary of the Central Medical War Committee to the Under-Secretary of State for War on the commissions now being granted to women doctors. At present women practitioners serving with the Army for the duration of the war are not officers of the R.A.M.C. In the opinion of the Central Medical War Committee they should be granted the same rank, status, and title as men, a women's branch of the R.A.M.C. being created if necessary. The present position constitutes a denial of an accepted principle of the medical profession, which recognizes no distinction between the sexes in the execution of professional duties.

SURGICAL PRINCIPLES IN DIVISIONAL MEDICAL UNITS

BY

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The work of divisional medical units under conditions of active service is mainly aimed at the efficient evacuation of casualties. It has become clear in the present campaign that a smooth and rigid scheme of treatment and evacuation from aid posts to casualty clearing stations as was possible in 1917-18 cannot be achieved. The medical services in the field must adapt their activities to events, and though it is impossible to forecast the circumstances under which individual units will work, the general principles of wound treatment should form the background of their action in relation to the individual wounded man. There is no doubt that the treatment he receives in the zone in question has a great influence on his subsequent condition, and an attempt will be made below to define what should or should not be done with a wounded man in regimental or field ambulance posts.

We started this war with a clear idea of the ideal wound treatment: this was founded on the experiences of 1914-18, and was to some degree coloured by reports on Spanish practice in their civil war. Since then experiences with our Expeditionary Forces and at home have done little to alter the established principles, though they have brought to light the value of the sulphonamide group of drugs in prophylaxis. Moreover, there has been activity on the research side both in relation to these drugs and into the value of antisera for anaerobic infections. The importance of fluid replacement in the treatment of shock has become fully recognized, and the provision of preserved blood or a substitute has been put on a sound basis.

Importance of Early Operation

Whatever adjuvants to wound treatment we may now possess nothing has lessened the proved importance of early operation for the majority of the wounded if serious infection is to be avoided. The operation in general will be one of débridement or the establishment of drainage, in accordance with the time-lag imposed and the surgical conveniences available. Primary repair is aimed at only for intra-abdominal injuries and those of the chest wall and skull. Primary suture of a somatic wound is not advisable except in very carefully selected cases. The ideal time for operation after the man has been injured cannot be defined with absolute precision. It is generally recognized that the period during which a radical excision or repair operation is likely to be satisfactory is within at most twenty-four hours of injury. Subject to the necessary period of resuscitation most authorities would reduce the ideal time-lag to twelve hours.

Our organization in the forward area is based, therefore, on getting the seriously wounded into the care of a surgical centre with the minimum of delay. The term "surgical centre" is used to imply any organization where formal surgery and the full process of resuscitation can be carried out. The difficulties in conforming to this ideal under the varying conditions of modern war are only too patent. We have to admit this handicap and aim at adaptability and elasticity in this matter as in other spheres of Army activity.

Treatment in Forward Units

The following may be laid down as the procedures to be carried out for the wounded at the aid post before transfer to the surgical centre:

1. A simple dressing of adequate size is applied to the wound if this has not already been done.

2. If the patient has not already received it, A.T.S. (3,000 units) should be given and the fact notified on his field medical card. The employment of anti-gas-gangrene serum at this stage may be of value, but a decision as to its general use has not been arrived at. Sulphanilamide may be administered to the more seriously wounded, especially in cases in which fractures are present. It should be given by the mouth, a 2-gramme dose to start with and 1 gramme at four-hourly intervals subsequently up to a total of about 20 grammes. A note as to the time the treatment started and the dosage given should always be entered on the man's documents for future guidance. The question of packing the wound with sulphanilamide is referred to below.

3. *Shock.*—The first need of the wounded man is for rest, warmth, relief of pain, and drink. Simple though these demands are in quiet periods, in forward units they cannot always be completely satisfied under conditions of activity. When achieved they go far to bring a man out of primary shock. Transfusion of serum or plasma will of necessity be limited by the conditions of the aid post and other circumstances. In general, it may be said that the transfusion of a pint of serum or plasma at this stage should be reserved for serious fracture cases or for those in which a severe haemorrhage has been controlled by ligature. For a serious burn similar treatment will sometimes be advisable before evacuation, but it is evident that the storage of the necessary material and the conditions for the proper administration of a transfusion will exist only in the larger aid posts.

The following notes are concerned with the treatment of special conditions.

Fixation of Fractures

Satisfactory fixation of fractures before evacuation is of the first importance if secondary wound shock and increased local damage are to be avoided. For fractures of the thigh and in the region of the knee the Thomas splint is of the greatest value. It should be applied in accordance with the recognized method, over the clothes with the boot and sock still in place. Traction is exerted through a clip or skewer attached to the boot or by binding the foot to a foot-plate. Traction should not be severe, nor should it aim at a complete reduction of any overlap of the fragments which may be present. A splint with a large-sized ring must be used for these cases, and therefore the result of forced traction is to push the ring up into the femoral angle, producing a condition that is both uncomfortable for the patient and liable to produce a pressure sore. The tension applied should only be sufficient to stabilize the fragments. The ring of the Thomas splint, when too large, can be to some extent stabilized by packing between the upper part of the thigh and the outer section of the ring. Judicious suspension of the ring from a suspension bar attached to the stretcher will also have the same effect.

Fractures of the tibia and fibula may be treated in the same splint. As a rule little or no traction is required, but control of the rotation of the lower fragment should be obtained by binding the foot to the foot-piece. In fractures of the lower half of the leg a simple box splint with a foot-piece is, I think, preferable. This can be made from Cramer wire splinting or, if this is not available, from boards or Gooch splinting. A similar arrangement should be employed for the splintage of injuries about the ankle or foot.

In the upper extremity, fractures of the humerus in the proximal half of the bone, and including injuries to the scapula, are best fixed by binding the arm to the side with a pad placed between the arm and the chest wall; the forearm is supported by a sling. If the fracture is in the lower half of the bone or about the elbow-joint the use of a posterior splint extending from the shoulder to the hand is desirable, the elbow being set at about a right-angle. This splint is most conveniently made from Cramer wire splinting. If it happens to be available a plaster-of-Paris slat instead of the wire splint will serve even better, but there must be no question of applying a complete encircling plaster bandage in this phase. Fractures of the forearm, wrist, and hand should be immobilized on a section of Cramer wire splinting bent at a right-angle to hold the elbow. It should be noted that fixation of fractures in this

stage aims at immobilization rather than rectification of position. It will be sufficient if the limb is aligned in its splint in approximately the normal position. Tight bandaging, especially of the forearm and about the elbow, should be avoided.

Fractures of both lower and upper jaws can for the purposes of early transport usually be adequately fixed with the four-tailed bandage. If there is a tendency for the tongue to fall back owing to complete destruction of the symphysis, a stitch or two should be used for either fixation or traction. A feeding-cup with a rubber tube extension on the spout will facilitate feeding. If possible the man should be transported in the sitting position.

Spine.—It has become customary to advise the transport of spinal injuries in the prone position. This position is very uncomfortable and distressing for a stretcher journey of any length. Moreover, it renders access for catheterization impossible without considerable disturbance. The theory supporting this practice is that extension of the spine is thereby maintained, the position of extension preventing vertebral displacement and tending to reduce any deformity present. The prone position certainly has the advantage that it prevents the formation of dorsal pressure sores, though not those on the ventral aspect. It is clear that missile wounds of the spine, whether associated with cord symptoms or not, are not subject to this argument. The same may be said of impacted flexion fractures. It is doubtful if the position is of much importance in the case of fracture-dislocations provided that gross flexion of the spine is not allowed to occur. It is therefore advised that spinal injuries should be transported in the supine position. The man should be lifted by three persons, one of them taking care to support the spine at about the level of the injury in such a way as to prevent flexion. On the stretcher the lumbar curve is maintained by a small cushion or folded blanket. For cervical injuries extension is sufficiently maintained by a similar arrangement placed just above the shoulder level. In spinal injuries and wounds in which the cord or cauda has been involved the important point in early treatment is the avoidance of pressure sores and infection of the bladder. Pressure sores on the heels are less likely to form if sock and boot are left on, unless the latter are wet through. If available an air ring should be put under the buttocks. When retention of urine is present a gentle attempt at expression should be made ; if this fails and the man is very uncomfortable catheterization may be carried out, but only if it can be done with aseptic precautions. If the case has to be retained for some days or if the period of transport is long, it will be well to tie the catheter in (Taylor, 1941).

Ribs.—If only a few ribs are broken the disturbance necessary for proper strapping should be avoided unless dyspnoea is extreme and the man is clearly unfit for transport. When many ribs are staved in it is best to strap the chest, completely encircling both sides. This fixation of the lower part of the chest will enforce diaphragmatic breathing, but it reduces the dyspnoea resulting from irregular chest movements.

Other Special Conditions

Amputations.—Primary amputation in the forward area should only be undertaken when the lesions of the soft parts are so gross or the damage to the main vessels is so complete that survival of the distal part is out of the question. If evacuation is good even when these conditions are present, operation should be deferred until the surgical centre is reached, so that a more formal procedure can be there carried out than is usually possible in an aid post. It is said that the development of secondary wound shock can be checked (M.R.C. War Memo. No. 1, 1940) in such cases by the application of a tourniquet immediately above the wound.

Chest Wounds.—Wounds in this area rarely require more than a surface dressing unless an open pneumothorax or sucking wound is present. In this latter event it is important to close the opening effectively. Suture with this in view should not be carried out unless complete wound excision can be coupled with it. A large greased pad covered with mackintosh tissue should be strapped over the opening (Barrett, 1940). Elastoplast will be most satisfactory for the purpose, but ordinary adhesive tape will serve. The strapping should overlap and extend over the whole pad. Occasionally an early pressure pneumothorax may be met with. Cyanosis and dyspnoea, together with displacement of the apex beat and sometimes the trachea, will enable a diagnosis to be made (Sellors, 1941). When it is recognized it should be relieved by needle puncture at once.

Abdominal Wounds.—In the ordinary way the wounds will be protected and the patient marked for early evacuation to the surgical centre. Morphine should be given in those cases in which diagnosis of perforation of the gut is evident from the position of the wound or from the clinical signs. No attempt should be made to return prolapsed viscera or omentum ; they should be covered with a normal saline pack or plain dressing and bandaged, a note being made of the state of affairs on the F.M.C.

Head Injuries.—A simple protective dressing only should be employed, even when there is prolapse of brain. A note as to the mental state of the patient and a record of the pulse and condition of the pupils or any paralysis which may be present should be made on the F.M.C.

Burns.—The treatment of burns in the initial phase is directed to preventing shock, which may prove fatal. If, however, the burn is of such a size as not to endanger life the main consideration is quick healing and the restoration of function. The danger to life from extensive burns is best treated by some method of surface coagulation. Tanning has proved the most satisfactory in this respect. The tanning is perhaps best effected with tannafax jelly or the application of compresses wrung out in 2% tannic acid. The latter method of application is most convenient in cases to be evacuated shortly. Smaller burns, and any burns of the face and hands, should not be tanned ; they should be powdered with sulphanilamide and then covered with vaselined lint or gauze. No attempt at surgical cleansing is made. There are several pastes on trial for application under these conditions, but it cannot yet be said that any have proved their superiority to the simple method suggested (E.M.S. Memo., 1941).

Haemorrhage.—As a serious problem haemorrhage does not appear as often in aid posts as one would expect from a perusal of first-aid treatises. No doubt if a major vessel is torn open a man dies before aid can be given, and he does not reach the aid post. If a medium-sized vessel is divided completely it has considerable capacity of retraction, and in the condition of shock which is produced by the injury self-sealing will very likely occur. When bleeding is obviously continuing from a wound an attempt should be made at the dressing station to control the bleeding-point with a ligature or forceps. If a tourniquet has been applied it is most undesirable to continue its use for longer than is necessary. In a large proportion of cases in which a tourniquet has been applied in the field haemostasis would have occurred without its use, for it takes place after the tourniquet has been in position for half an hour or so. For haemorrhage from minor vessels firm pressure exerted by a pad bandaged in place, coupled with recumbency, will often suffice for control.

Priority in Evacuation.—When evacuation is normal and the journey to the surgical centre can be effected in about an hour abdominal injuries should have precedence. Fractures and sizable retained foreign bodies should come next, and chest and head injuries last. If the pressure of casualties is very great this order will clearly have to be altered, and the alteration must be determined by the medical officer on the spot, since he has a knowledge of the local conditions and surgical possibilities.

Isolation of an Aid Post.—When evacuation is impossible and an aid post is isolated and therefore saddled with the responsibility for the wounded over possibly a period of several days, it is clear that an attempt should be made to produce the conditions of a surgical centre. In fact, this will not often be practicable on account of the lack of personnel and of the necessary amenities. Formal or radical operations for abdominal wounds will seldom be carried out,

and the same may be said for chest and head injuries. The surgical treatment of open fractures will be directed to effecting free drainage rather than radical wound excision. Amputations should be carried out for gangrene or for local infections which may threaten life.

Pansement d'Attente.—The main efforts of available personnel should be directed to the prophylactic use of sulphanilamide for all serious wounds—or, if circumstances permit, all wounds. This treatment should be made effective as soon as possible. From 5 to 20 grammes should be introduced into each wound, according to its size; a total of 40 grammes should not be exceeded in any individual. Enlargement of the wound may be necessary to give complete access. Foreign bodies which have been located and are easy to remove should be extracted at this stage. The powder should, so far as is possible, be brought into contact with the whole wound surface or track; it should not be tightly packed in. An insufflator, if available, may be used; but it would appear that introduction with a small spoon of known capacity is more convenient. If instead of powdered sulphanilamide the tablets are used, the latter should be crushed before introduction in order to facilitate absorption by the tissue fluids. The prophylactic use of the drug by mouth as detailed above should be reserved for cases in which the development of serious infection is deemed probable: missile fractures and irregular retained foreign bodies are instances which would come into this category.

Summary

The above is a brief outline of the surgical principles which should determine our treatment of the wounded man in the forward area, together with an attempt to summarize practice. In war any set plan can seldom be carried through in every detail. We should have a clear conception of the ideal at which we aim, and in action do our best to attain it despite unforeseen difficulties and inevitable handicaps.

I should like to acknowledge my indebtedness to Brigadiers F. Laing and E. M. Cowell and to Colonels J. Weddell and L. Colebrook for useful suggestions and advice in the preparation of this memorandum.

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WORK OF THE LISTER INSTITUTE

STUDIES OF VITAMINS IN WHEAT FLOUR

It is fifty years since the Lister Institute (then called the British Institute) of Preventive Medicine was incorporated, but as active work did not begin until 1893 any jubilee commemoration is postponed until the year after next, by which time it is hoped that the dawn of peace will be stimulating research in every field. Meanwhile the report of the Governing Body for 1941 contains an account of much interesting work. Probably the studies on accessory food factors claim the most immediate importance in view of the food situation in this country.

The Division of Nutrition, which is located at Cambridge, has been devoting its energies to filling the gaps in knowledge which still exist as to the nutritive value of different portions of the wheat grain. The flour generally used in this country for making white bread represents 73% of the wheat grain, the remainder being discarded and used for animal feeding. Wholemeal flour (100% extraction) has been shown to be richer in mineral constituents and to contain more vitamin B_1, more of the vitamin B_2 complex, and proteins of higher nutritive value than white bread. But some of the previous investigations are based on results which could be criticized in the light of more modern methods, and therefore it was thought desirable to investigate further the digestibility of bread made from wholemeal and white flour respectively, the relative nutritive value of the proteins contained in each, and their content of the different members of the vitamin B_2 complex.

Superiority of Wholemeal

So far as digestibility is concerned, the observations were made on six volunteers who for ten or eleven days consumed diets consisting almost entirely of bread made from the different types of flour. In the white bread ingested, "5% of the energy" and 9% of the nitrogen was found in the faeces, the corresponding figures for the wholemeal bread being 13 and 14% respectively. It is calculated that in the manufacture of white flour about 20% of the total energy available to man in the wheat berry is discarded, while of the nitrogen 27% goes into the offals. None of the subjects was adversely affected by the wholemeal breads, of which they consumed 2 to 2½ lb. daily.

The nutritive value of the proteins of white and wholemeal flours was studied by comparing the growth of young litter-mate rats. After adjustments had been made to secure a fair comparison, the rats on wholemeal diets were found during the observation period of nine weeks to have a weight increase nearly twice that of rats on the white-flour diet. A 30% superiority in nutritive value for the proteins of the whole wheat was confirmed by other experiments. Similar experiments on rats were carried out to determine the value of B_2 vitamins in the flours. The diets were made equal in other respects, but the rats receiving the white-flour diet, even though fortified with vitamin B_1, showed a rate of growth which was only about one-half that of the group receiving the wholemeal. The superiority is attributed to the higher content of B_2 vitamins in the wholemeal as compared with the white flour.

Some work has been done on the fat-soluble vitamins in wheat flour. In the process of milling a considerable part of the fat contained in the germ of the wheat grain is disseminated throughout the flour. The fat-soluble vitamins present in this oil are provitamin A (carotenoids) and vitamin E. The biologically active fraction of provitamin A is very small, so small that rats living on a diet composed almost entirely of flour failed to obtain sufficient to protect them from vitamin-A deficiency. Wholemeal flour is no richer than white flour in this respect. The bleaching of flour to get rid of its creamy colour destroys the carotenoid pigments, but the amount is so small that it cannot be regarded as a serious nutritive loss; the possible damage to other nutrients, especially vitamin E, is under investigation.

Yeast as a Human Food

The nutritive value of yeast, with its high content of B vitamins, has been studied, more particularly the supplementary value of the B vitamins of the type of yeast known as *Torula utilis* to those in straight-run white flour. The addition of 2½% yeast to white flour makes it as good a source of B vitamins as wholemeal flour, and the addition of 5% makes it a better source. This amount of yeast may be added to white or wholemeal breads without seriously affecting their palatability, and in soups, meat and vegetable stews, and many other dishes yeast may be added in reasonable amounts with advantage. Work done on vitamin C showed that tomatoes grown in the open had markedly more antiscorbutic potency than those grown under glass. Some biological tests have been carried out on strawberries, the jam of which is popular and can be made available at times of the year when natural vitamin C is not so plentiful as at others. The antiscorbutic potency has been found to be of the same order as that of citrus fruits.

Serological and Biochemical Studies

Only the briefest reference can be made to much other research work. An inquiry has been held into the toxicity for mice of *Cl. welchii* strains from war wounds and air-raid casualties. While there is little doubt that the more toxic strains are likely to exert a more harmful effect upon the resistance of the patient than the less toxic, it is equally clear that even the least toxic are capable of setting up gas gangrene. The main source of danger lies in the conditions obtaining in the wound.

Experiments have been continued on antityphoid vaccination, especially with a view to preserving the Vi antigen. It has now been found that a vaccine that is not only killed with alcohol but preserved in it still contains the Vi antigen in its effective form after storage in the cold for at least nine months, and probably much longer.

In some work on the antigenic complex of *Bact. dysenteriae* (Shiga) it has been shown that agar, which by itself is non-antigenic, can be rendered antigenic by combination with the polypeptide components isolated from the antigen of this organism or the O form of *Bact. typhosum*.

The study of the manifold effects of sex hormones has been proceeding. One point investigated is whether oestrogenic hormones are necessary in the male organism for the normal development of the sex organs. In the male organism such large quantities of this female hormone are produced that some consider that for the commercial manufacture of oestrone the urine of the stallion is a better source than that of the mare. Therapeutic treatment with oestrogens of male patients suffering from prostatic hypertrophy has been advocated. The Lister Institute workers, however, find that when administered simultaneously with male hormones, oestrogens produce a very small increase in the development of the sex organs as compared with that which can be produced by increasing the dose of male hormone alone. It is concluded that the female hormone is not only unnecessary for the normal development of the sex organs in the male organism but may be harmful in view of the pathological (including precancerous) changes which oestrogens produce, and in any case its therapeutic application in the treatment of diseases of the male sex organs is not warranted.

To the National Collection of Type Cultures of Micro-organisms, which is housed at Elstree, 150 strains, many representing new types, have been added during the year.

MINISTRY OF HEALTH STAFF

The following appointments and promotions in the medical staff of the Ministry of Health have recently been made by the Minister of Health:

Senior Medical Officers: E. L. Sturdee, O.B.E., M.R.C.S. (in charge of the Regional Medical Organization, including environmental hygiene; succeeded Dr. H. A. Macewen, O.B.E., who has retired from the service of the Ministry). W. A. Lethem, *M.C.*, M.D. (Food and Nutrition).

Principal Regional Medical Officer of the London Region: M. D. Mackenzie, M.D.

Deputy Senior Medical Officers: N. M. Goodman, M.D., C. J. Donelan, M.B., Miss G. I. Brodie, M.B., V. D. Allison, M.D.

Regional Medical Officers: G. V. Davies, F.R.C.S., D. L. MacKenna, M.B., W. G. McKenzie, *M.C.*, M.R.C.S.

The German journal *Archiv für Schiffs- und Tropen-hygiene* has with the new year changed its name to *Deutsche Tropenmedizinische Zeitschrift*, and will in future appear fortnightly instead of monthly.

BEIT MEMORIAL FELLOWSHIPS

A meeting of the trustees of the Beit Memorial Fellowships for Medical Research was held on July 23. It was noted that out of the thirty present Fellows thirteen had already been seconded at their own request for more direct service during the war, and six others have undertaken some research work for Government Departments on problems arising out of the war.

Election of New Fellows

The following elections were made, all with permission for each Fellow to be seconded at any time for war duties:

Senior Fellowship (£700 a year).— T. R. R. Mann, M.D.Lwow, Ph.D.Camb. To continue his work on intracellular metallo-protein compounds, especially of red blood cells, at the Molteno Institute of Biology, Cambridge University.

Fourth-year Fellowships (£500 a year).—J. F. Danielli, B.Sc., Ph.D.Lond. To continue his work on the permeability of muscle fibres and of capillaries, at the Biochemical Laboratory, Cambridge University. Miss C. O. Hebb, M.A.Dalhousie, Ph.D.McGill. To continue her studies of physiological problems in relation to high altitudes, at the department of physiology, Edinburgh University. H. Lehmann, M.D.Basle, Ph.D.Camb. To continue his work on the influence of shock and of the suprarenal glands on glycogen synthesis, at the Biochemical Laboratory, Cambridge University.

Junior Fellowships (normal value £400 a year).—E. F. Gale, B.Sc. Lond., Ph.D.Camb., Fellow of St. John's College, Cambridge. To study bacterial amine production as a cause of non-specific infantile diarrhoea, at the Biochemical Laboratory, Cambridge University. W. Holmes, B.A.Oxf., Senior Demy of Magdalen College. To study the regeneration of nerve fibres after injury, at the department of zoology, Oxford University. Miss M. F. Lockett, M.D.Lond., M.R.C.P. To identify renal pressor substances responsible for experimental high blood pressure, at the Pharmacological Laboratory, Cambridge University.

Reports of Societies

YELLOW FEVER IN AFRICA

At the annual general meeting of the Royal Society of Tropical Medicine and Hygiene, with the president, Sir RICKARD CHRISTOPHERS, F.R.S., in the chair, a paper was read by Dr. G. M. FINDLAY on the present position of yellow fever in Africa.

Dr. Findlay said that recent events had clearly demonstrated the specificity of the mouse-protection test for immunity to yellow fever in the blood of human beings, and had shown that the area which had been marked out by this test as the endemic zone in Africa coincided very closely with the actual distribution of yellow-fever cases. The endemic zone now extended from the west coast of Africa just to the north of Cape Verde, along the southern border of the Sahara to the Anglo-Egyptian Sudan, and thence, bending southwards, it crossed the White Nile and extended as far east as, and quite possibly beyond, the Sudan-Abyssinian border; the eastern border of the area extended southwards through the western part of Uganda, and thence diagonally across the Belgian Congo to the mouth of the Congo River. Any area in this zone was liable to be the site of an explosive outbreak of yellow fever.

Three epidemiological types of yellow fever could be recognized in Africa—urban epidemicity, rural epidemicity, and rural endemicity. The first type was carried on by *Aëdes aegypti* and was apparently due to the importation of yellow fever from the country into the town; in the second type it was impossible to exclude *A. aegypti* as a vector, as this mosquito was so widely distributed throughout rural Africa. The factors favouring rural endemicity were as yet unknown. It seemed most unlikely that infection could be maintained solely by the man-mosquito cycle. Although 20% of wild monkeys in the endemic zone were known to contain immune bodies in their blood, it was not considered likely that monkeys were sufficiently numerous to carry on infection in the absence of man. The possibility of other alternative hosts must therefore be considered. So far no wild animals other than one ostrich had been found to possess immune bodies in their blood, although in Columbia marsupials and certain other wild animals had been found to possess an acquired immunity. The sera of

numerous domestic animals in Africa—cows, sheep and goats, horses, pigs, dogs, and a camel—have been found to contain virucidal bodies against yellow-fever virus. The specificity of the mouse-protection test as applied to animals required further investigation, but the results so far obtained were suggestive. The possibility of a reservoir other than the mosquito but with a longer life could not altogether be excluded. The two chief problems in relation to yellow fever in Africa were the more efficient control of yellow fever in the endemic zone and the prevention of the spread to East and South Africa, with further extension to India and the Far East. Infection could be carried either by the infected mosquito or by the infected human host. Owing to the greater rapidity and the greater volume of traffic there was now much more chance of the virus spreading from the present endemic area and being carried either by plane, motor car, ship, or train to non-endemic areas. If infection reached East Africa there was at present a considerable chance of its passing across to Southern Arabia and India, because the dhow traffic was a replica of the shipping which during the seventeenth and eighteenth centuries carried yellow fever between Africa and America.

The methods of preventing the extension of yellow fever comprised more concentrated attacks on the breeding of mosquitos and more efficient control of aerodromes and of persons travelling by car from endemic to non-endemic zones. In immunization was to be found a most efficient means of prevention, and it was quite time that regulations were promulgated to forbid the residence in any yellow-fever area of any non-African who had not been immunized against the disease. In certain selected areas mass immunization of the whole population must be considered. At present the greatest difficulty in the efficient control of yellow fever lay in the multiplicity of authorities, each of whom was concerned solely with the condition of affairs within his own borders. Until there was a greater correlation of administrative effort yellow fever would continue to be a menace to the health of Africa and of the whole tropical world.

General Discussion

Dr. HUGH SMITH (International Health Division of the Rockefeller Foundation), who had recently been in charge of yellow-fever investigations in Colombia, gave a brief account of the present position in South America. In the past three years there had been no instance of an *Aëdes aegypti*-transmitted outbreak, although there had been many outbreaks of jungle yellow fever. In Colombia yellow fever recurred again and again at intervals of one or more years in the same isolated valleys, often within a short distance of a previous outbreak. Intensive studies had been made of all outbreaks, and so far no other arthropod than mosquitos had been found infected. On eight occasions, however, virus had been isolated from wild *Haemagogus* mosquitos. It was very difficult to account for the continuance of yellow fever in these areas, some of which were practically uninhabited. A high percentage of monkey blood, however, was positive for yellow fever, thus strongly supporting the suggestion that yellow fever could maintain itself in the absence of man. Although yellow-fever virus did not pass from one generation of *Aëdes aegypti* to another through the egg, it was possible that this might happen with other mosquito vectors, and this question was now being investigated. The absolute impossibility of diagnosing yellow fever on clinical grounds was stressed. In eradicating yellow fever it was essential to combine immunization with eradication of *Aëdes aegypti*; it was not, however, always easy to immunize a high percentage of the population. Efforts were now to be undertaken to eradicate *Aëdes aegypti* from the whole of the Amazon Valley.

Colonel F. P. MACKIE drew attention to the difficulties imposed on air travellers by the differing regulations in force in different countries. Some countries accepted a certificate of non-exposure for six days; others insisted that if a person had been immunized against yellow fever he could not be admitted for ten days, while others extended the period to twenty-one or twenty-three days. Colonel T. MENZIES asked if combined vaccination against small-pox and yellow fever was recommended. It had been practised in certain French colonies. Dr. H. S. STANNUS said that he had never seen a case of blackwater fever in an African, although such cases had been recorded. He suggested that they might in reality have been cases of yellow fever. Prof. T. F. HEWER drew attention to the difficulty in diagnosing cases of acute and subacute liver necrosis from yellow fever. Such cases, which were not uncommon, might in Africa be associated with black vomit. Brigadier RICHARDSON asked if there was any truth in the suggestion that dengue immunized against yellow fever.

Dr. FINDLAY, in reply, said it was now generally agreed that persons who had been inoculated against yellow fever were immune to the bite of an infected mosquito ten days later. There was absolutely no scientific justification for imposing quarantine periods of twenty-one days or over. Dr. HUGH SMITH concurred in these statements. It was impossible for anyone who had lived in an endemic zone to say that they had not been exposed to yellow fever, and certificates of "non-exposure" granted by any country in the endemic zone were therefore farcical. So long as immune bodies could be shown to be present in the blood by the mouse-protection test there was no need for re-immunization. If it was impossible to have a mouse-protection test carried out it was advisable to be re-inoculated every two years, although there was considerable evidence to show that anyone who had ever had immune bodies in his blood was immune for a considerable number of years. Combined inoculation by scarification of vaccinia and yellow fever was not favoured. Dengue and yellow fever gave no cross-immunity.

NASOPHARYNGEAL DISEASE IN MENTAL DISORDER

At the one hundredth annual meeting of the Royal Medico-Psychological Association, held in London on July 17, a discussion took place on diseases of the ear, nose, and throat in mental disorder.

Dr. T. G. GRAVES, president of the Association, said that the region of the ear, nose, and throat was a part of the body where there was the greatest concentration of functionally differing nerves and end-organs and other essential lines of communication, and this area also, from the point of view of absorption, formed the beginning of the visceral sheath. Here, therefore, disease, effecting positive and negative disturbances of sensation, could in the mind confused by toxaemia emanating from the same source produce an erroneous conception of environment. He added that clinicians who professed interest in the chronic infective process seemed to regard its importance very differently. For example, quite recently two important but separate clinical reviews had covered the subject with the sentence, "Of course, obvious septic foci should be removed." The adjective "obvious" seemed a meaningless and therefore unnecessary qualification.

Mr. H. G. BEDFORD RUSSELL said that it was often forgotten that the earlier response on the part of the tissues to infection with streptococci was the production of oedema, not pus. The presence of pus might be misleading in the establishment of the diagnosis of sinusitis. The phenomenal power of swelling possessed by the sinus lining resulted in localized pains in various parts of the head. The generalized headache might be understood when it was recalled that the trigeminal nerve supplied the meningeal as well as the nasal sinuses. There was considerable evidence that migraine was associated with an urticaria of the sphenoidal lining rather than inflammation thereof. He described a number of cases in which nervous disorder had been associated with unsuspected nose trouble, with oedema of the sinuses. There was a flavour of mental disorder about the symptoms of many patients who consulted rhinologists—he believed that this was more marked than among the patients who consulted gynaecologists. A typical trouble among these patients was carcinophobia.

Septic Absorption from Sinuses

Mr. ERIC WATSON-WILLIAMS said that the nasal accessory sinuses were, more often than the ear, the source of chronic septic absorption which caused trouble regarded as neurotic. Of the last 200 private patients seen by him who proved to be suffering from nasal sinusitis 87 complained of what might be

called a "toxic neurosis." Chronic toxic absorption produced a very definite effect on the mentality, often perhaps mild, but not seldom profound, and sometimes going beyond the borders of what a fairly tolerant public considered sanity. In the watch for focal infection it was not enough to pay regard only to the obvious sources, the teeth and tonsils; the ear should not be ignored, and a complete investigation should be made of the nasal accessory sinuses.

Mr. J. C. HOGG said that it must not be supposed that the rhinologist was often confronted with an obviously psychotic patient, but one could not help wondering how much incipient mild mental disorder was overlooked in a busy clinic. It was easy to take the view that sinusitis was due to pus, and that if there was no obvious pus there could not be sinusitis; but rhinology did not lend itself readily to over-simplification. Very slight pathological changes in the membranes lining the nasal sinuses would often give rise to severe and crippling headache; on the other hand, there might be widespread disorganization of the nasal sinuses without any pain whatsoever. Mr. R. S. STRANG said that he was quite convinced from the results he had seen that considerable amelioration or even cure of mental states could be obtained by the removal of chronic infective conditions of the ear, nose, and throat, even when such conditions were not obvious. He regarded a complete investigation of this region in mental patients as offering some hope of improvement. Mr. S. E. BIRDSALL said that the rhinologist saw a large number of cases of sinusitis, but in only a few of them could mental disorder be said to exist. Out of 80 such cases at a children's hospital, only 5 had been referred on account of what could be described as mental symptoms, such as listlessness, inattention, and excessive fatigue. School medical officers in their reference of cases evidently had in mind a connexion between being a dunce and having large tonsils, but in very many cases he thought it could be shown that the sinuses and not the tonsils were at fault. With regard to the ear, he believed that among deaf-mutes mental depression was uncommon; the deaf-mutes whom he happened to know were exceptionally happy and lively people. But it was very different with the person with acquired deafness of high degree (leaving on one side senile deafness), who was usually introspective, morose, depressed, and ill adjusted.

Dr. F. A. PICKWORTH, who gave a lantern-slide demonstration of pathological conditions, said that infection of the sphenoidal sinuses was not *per se* a cause of mental disorder, but was a source of vascular changes in the brain. He believed that such vascular changes inhibited neuron integration by obstruction at various synapses, so that the pattern of motor behaviour was rendered abnormal, and that clinical mental disorder became evident when such vascular changes were extensive or had a certain anatomical localization. Dr. H. F. FENTON said that as the superintendent of a mental hospital he had formed the firm opinion that cases of toxic infection did occur among mental patients, and that chronic as well as acute cases could be successfully treated. When focal sepsis was found and eradicated mental and physical improvement ensued in the majority of cases; in many the response was remarkable, and in those in which recovery did not occur there was generally a reduction in psychomotor activity, better behaviour, and improved health. Dr. ARTHUR POOL asked why, although practically the whole population suffered from colds, only a small percentage developed sinusitis. He suggested that a good many patients got and maintained their infection because they had not the right diet which enabled them to withstand the infective process. Before any patient was subjected to the severe operations which had been outlined he should be given the benefit of medical treatment, with the administration of adequate quantities of vitamin C, together with a regulation of the salt content of the diet. Dr. W. J. T. KIMBER wondered whether the change in the atmosphere and spirit of a mental hospital in which these methods of investigation and treatment were introduced might not have a psychological effect which in part explained the results. The more hopeful treatment of patients was in itself a valuable factor.

Dr. ASTLEY COOPER referred to some statistics circulated by the president, from which it appeared that out of a total of 3,050 patients, nasopharyngeal sepsis had been found in 2,754 (over 90%). This meant either that it was a universal cause of mental disease and that its eradication ought to produce recovery or that the very universality of the condition made it negligible as a cause. "Improvement" appeared to be as inevitable as in all the recently introduced "successful" treatments of schizophrenia.

Dr. A. A. W. PETRIE (president-elect of the Association) said that he was not entirely convinced that ear, nose, and throat trouble was the most important cause of mental disorder, but he shared with other medical superintendents the view that intensive investigation of patients for signs of focal sepsis was entirely to the good.

Local News

ENGLAND AND WALES

Mental Welfare

In the early part of 1939 the Mental Health Emergency Committee was constituted to function, in the event of war, in order to prevent the overlapping of mental health services. It included representatives of the Central Association for Mental Welfare, the Child Guidance Council, and the National Council for Mental Hygiene; later on representatives of other bodies were added. In its first report, covering a period of two and a quarter years, it describes the assistance its mental health workers have been able to render in reception areas among children who have been evacuated. The value of such work in its experimental stage was brought home to the Ministry of Health, which agreed to recognize the payment of these workers as an evacuation expense. A survey was made of the hostels for difficult children, and, with the beginning of intensive raids, help was given in the shelters and rest centres, as well as in the receiving areas in which the homeless people, especially those suffering mentally or nervously from the result of raids, were subsequently billeted. The Central Association for Mental Welfare, which also issues its report for two years, has to confess to some enforced suspension of activity, but it has been in a position to institute lectures on psychology to teachers, to arrange a course for medical practitioners, to help in arranging special billets for mentally unstable, subnormal, or senile individuals whose condition has been rendered more acute through shock, fear, or the destruction of their homes, to continue the visitation of epileptics in London and the Home Counties, and to carry out much other useful work. It is regretted that the report of the Feversham Committee on voluntary mental health services should have had to be shelved, but it is felt that the co-operation which has come about between mental health bodies as a result of the war has vindicated the recommendations of the report to a degree which would have been impossible to attain by ordinary propaganda alone. When the pages of the Feversham report are reopened and their contents publicly discussed "the discussion will be carried on in the light of incontrovertible practical experience, and the battle—if battle there be—will have been half won at the outset."

Appeal for London Hospitals

An appeal for £125,000 a year for hospitals during present circumstances was made at the annual meeting at the House of Lords of the King Edward's Hospital Fund for London, at which the President, H.R.H. the Duke of Kent, took the chair. The Duke of Kent said that uppermost in everyone's minds to-day, when they thought of hospitals, was the large number which had been bombed, and the endurance and bravery shown by the staffs as well as by the patients. The number of hospitals in the Metropolitan area, in which the Fund made its distribution of donations, which had been severely damaged now totalled 43, while a further 30 had been less seriously damaged in air raids. The Duke continued: "From what I have seen myself of hospitals in London and elsewhere, I can endorse all that has been said about what they have suffered and the way they have stood up to it. We are all specially grateful for the practical expression of sympathy which has come from our friends in the United States. . . . Our annual report refers to the schemes of some of the hospitals for moving part of their civil work to the country.

The King's Fund is watching this experiment with sympathy and interest, particularly because of the financial liabilities implicit therein. The King's Fund has already given additional help to the hospitals in the difficulties caused by the war and the conditions preceding the war. The annual distributions, both for 1939 and for 1940, were maintained at £300,000. Emergency grants totalling £80,500 were also made to a few hospitals during these two years. The combined result was that the total of grants and special administrative services was £307,000 in 1939 and no less than £384,000 in 1940." Reference was made to the work of the Voluntary Hospitals Parliamentary Committee, which included members of the King's Fund, the Nuffield Trust, and the British Hospitals Association, in presenting the case of the voluntary hospitals in connexion with Workmen's Compensation, the Purchase Tax, and the War Damage Act.

Hospital Contributory Schemes

Steps to increase and co-ordinate hospital contributory schemes are to be taken by a new representative committee set up by the King Edward's Hospital Fund for London. Contributory schemes have grown rapidly during recent years until they now provide an important part of the income of voluntary hospitals. Sir Kenneth Wigram, who is also connected with the Nuffield Hospital Trust, is the chairman of the new Contributory Schemes Committee, which includes representatives from the Voluntary Hospitals Committee, the Hospitals Savings Association, and the Hospital Saturday Fund. The Committee will examine the different schemes in the metropolitan area, making recommendations, and will also deal with the relation of London hospitals to schemes in the Provinces. The secretary is Mr. T. W. Place, for some years secretary of the British Hospitals Contributory Schemes Association.

Birmingham Accident Hospital

Since April last the Queen's Hospital, Birmingham, has become the Birmingham Accident Hospital and Rehabilitation Centre. Certain of the medical, nursing, and administrative staff have been taken over, as well as the buildings and equipment, and thus a specialized hospital has been established devoted entirely to the treatment and rehabilitation of men and women injured as a result of accident. The Board of Management has appointed Mr. William Gissane, F.R.C.S., of St. James Hospital, Balham, to be clinical director, and he is expected to take up his duties early in September. He will be assisted by a full-time staff with specialized knowledge, and a number of consultants will be associated with the work. The operating theatres, plaster rooms, and *x*-ray services will be available at all hours. There are 280 beds, certain of which will be set aside for observation cases in order that patients suffering from wounds may have a short period of in-patient treatment to ensure that complications will not develop. Rehabilitation by remedial exercises and occupational therapy will be carried out in a department to be set up for the purpose. Schemes have been prepared by the Board for the establishment at this hospital of schools for the training of nurses in industrial nursing and of selected personnel for industry and industrial first aid. The provision of a mobile surgical unit is also part of the Board's policy.

Merseyside Hospitals Council

The report of the Merseyside Hospitals Council for 1940 states that the income last year soared to a new high record of £280,284. The employers subscribed £46,220. In the three years immediately before the war the amount which it was possible to pay to the voluntary hospitals had each year fallen short by an average of £47,500 of the actual cost of the hospitals' services to members and their dependants—a sum very like that by which the hospitals collectively failed to balance their budget each year. This amount was made up during 1940 partly as a result of a plan known as the extra penny—whereby members subscribe not only a penny a week for every £ but for every part of a £—and partly because of the sharp upward curve in employment. Last year the associated voluntary hospitals received £113,246, which was £2,138 more than was distributed to them in 1939, leaving a balance of £47,000 from the year's revenue, which was held back for very good reasons. Some of the hospitals have moved to new quarters, others have suffered in air raids, and in the closing months of the year their many and varied needs were not clearly known. Therefore the Distribution Committee, after discussing the financial position in all its aspects, decided to suspend the distribution of this reserve at least until the hospitals' financial position was known as at the end of the year 1940. Other items in the distribution were £33,104 for treatment in municipal hospitals, £14,667 to voluntary medical institutions other than the associated hospitals, £10,604 to civic war charities, and £9,400 to the medical staffs' fund. The offices of the Council have been moved to 40, Upper Parliament Street, Liverpool, their former headquarters having suffered air-raid damage.

SCOTLAND

Orthopaedic Progress in Scotland

At the annual meeting of the Princess Margaret Rose Hospital for Crippled Children, held recently in Edinburgh, Mr. W. A. Cochrane, the surgeon in charge, speaking of the success of treatment, said that many instances of notable achievements could be supplied. Sufferers from infantile paralysis had been cured, and in a number of very severe cases had been enabled to walk and lead an independent life. Deformed feet had been reconstructed and shortened legs restored to normal length. Upwards of 75% of the crippling conditions of childhood could be cured sufficiently for the child to grow up in a position which enabled him to earn his living on more or less equal terms with normal people. Besides carrying out its main purposes, the Princess Margaret Rose Hospital had been extended to provide for orthopaedic war casualties in the civilian population and in the Forces. Dr. Andrew L. Davidson, Chief Medical Officer of the Department of Health for Scotland, paid tribute to the hospital for its pioneer work in orthopaedics and its efficient organization. The care of the cripple, he said, was not only a medical but a social problem. The ideal to be aimed at was the prevention of crippling. Hitherto welfare work for cripples in Scotland had been backward and limited in scope, but even in these difficult times steps were being taken to establish regional orthopaedic schemes to cover the whole country.

An Edinburgh Nutrition Inquiry

The Edinburgh branch of the Children's Nutrition Council recently sponsored an inquiry into the adequacy of incomes and expenditures of 103 families with slender means, and has now issued a report entitled "Food and the War." The B.M.A. minimum diet, as laid down in the 1933 report of the Committee on Nutrition, was used as a basis for the inquiry, the items of food being repriced at their cost in Edinburgh in November, 1940. The income level of the families investigated was that of the unskilled labourer. The report states that the cost for an adult man had risen since 1933 from 5s. 11d. to 12s. 6d., the rise for children was rather less, but on the whole food prices for a family were about doubled. Out of 76 families whose food bills were examined, only eight are regarded as spending enough to buy a diet adequate in every respect. The main cause of the inadequacy was lack of means; other factors were imperfect catering or inability to obtain a sufficient variety of foodstuffs. In achieving even the low nutritional standards brought to light, half of the families were over-spending their income and running bills from week to week with shopkeepers. The children, according to this report, suffer from lack of essential protective foods and may show the stigmata of stunted growth, deficiency diseases, and an inability to withstand the ravages of infections. While much could be done by furthering the knowledge of correct eating and the best possible use of available food in the homes, the main task is to ensure that enough food of the right kind is obtainable by all. Four measures are advocated: a wide development of communal feeding, expansion of all social services relating to food, extension of the National Milk Scheme to include children up to the age of 16 at least, and distribution of certain vitamins as a social service. Greater use should be made of Scotland's agricultural potentialities. A more equitable distribution of available foods is called for, and steps should be taken to ensure that wages, allowances, and old age pensions keep pace with rising costs of living. Copies of the report may be had from the Secretary, Children's Nutritional Council, 37, Esslemont Road, Edinburgh, 9 (price 3d., by post 4½d.).

Correspondence

Radiodermatitis

SIR,—There is good reason to believe that the risk involved in setting fractures or removing opaque foreign bodies under the fluorescent screen is not generally appreciated, and as the practice appears to be on the increase the Council of the Faculty of Radiologists desires to draw attention to this risk.

That the risk is a real one is shown by reports of cases of *x*-ray dermatitis of the hands and faces of surgeons in the E.M.S. in this country. There is also a report from Leddy and Rigos from the Mayo Clinic (*Amer. J. Roentgen.*, May, 1941, p. 696). They record fifty-five cases of *x*-ray and radium dermatitis in doctors in the period 1919-34 and eighty from 1934-9. Of the latter group only five were radiologists and the remainder physicians and surgeons. Of these eighty cases fifteen were the result of *x*-ray therapy and the balance occupational—that is, resulting from diagnostic procedures or handling radium. Forty-six cases (only three being radiologists) were directly due to manipulations under the screen—either setting of fractures or removal of foreign bodies. In thirty cases the injuries to the hands have gone the length of ulceration, twenty-one of the ulcers being malignant.

As no screen apparatus in use at present, not even the recent model using indirect vision, can protect the hands against the rays if the fractured limb is being manipulated or the foreign body being removed while the current is on, these two procedures should be actively discouraged. In both, the operator's hands are inevitably exposed to the direct beam of the rays. The Council of the Faculty is of opinion that these methods should be used only in very exceptionally difficult cases, and that, when used, the manipulation and viewing with the current on should alternate so that the hands are never in the direct beam. The Council also recommends that a radiologist well versed in the factors involved should be in attendance when these methods are used. Further safeguards are the use of an adequate filter, small milliamperage, and low kilovoltage—for example, 2 mA at 55 kV peak. Experiments show that the output is very greatly reduced if these factors are adopted.—I am, etc.,

M. H. JUPE,
London, W., July 24. Honorary Secretary, the Faculty of Radiologists.

Cardiac Arrest during Anaesthesia

SIR,—Mr. Hamilton Bailey's admission (July 19, p. 84) that he has performed cardiac massage on forty patients whose hearts "suddenly and unexpectedly became still during general anaesthesia" provides a terrible indictment of his anaesthetic service. Such a host of catastrophes could only result from grossly incompetent anaesthetists or, and far more probably, from the widespread use of chloroform.

Prevention is surely better than cure, especially since the cure was successful in only 10% of the cases. With all deference, may I suggest that Mr. Hamilton Bailey would do his patients a greater service by forbidding the use of chloroform in his theatres, except when it is specially indicated, than by drawing up rules of procedure to be adopted when the use of this drug has already caused complete cardiac arrest.—I am, etc.,

Manchester, July 19. H. J. BRENNAN.

SIR,—Mr. Hamilton Bailey states (July 19, p. 84) that he has performed cardiac massage about forty times: only four patients have survived. One would be interested to know what type of general anaesthetic was administered, and particularly whether chloroform was used in any, or many, of these cases.—I am, etc.,

Dundee, July 19. F. R. BROWN.

SIR,—Referring to the subject, "False Anaesthesia in Childhood," to be discussed by a body of anaesthetists, the late J. H. Nicol said he would prefer to entitle it "Anaesthetists' Incompetence." I was reminded of that remark by the very frank paper by Mr. Hamilton Bailey on cardiac massage for impending death under anaesthesia, and was surprised that, in times when the administration of anaesthetics has passed almost entirely in hospital and nursing-home practice to the specialist, he should have found it necessary to perform cardiac massage "about forty times." If such an extreme procedure for resuscitation were so often necessary, how many times more must Mr. Bailey's work have been interrupted by the need for measures short of cardiac massage! That raises in my mind the question, "Has the competence of the anaesthetist kept pace with the increasing bulk of his plated paraphernalia?"

To one having come from a chloroform school, where, in the present view, mishaps would be expected to have been more numerous than to-day, it is astonishing that in these days of specialist administration any surgeon should be so unfortunate as to be called on to perform cardiac massage so often. Has Mr. Bailey been unfortunate in his choice of anaesthetists, or has he himself a penchant for this surgical procedure? As a general practitioner I do not feel competent to answer; perhaps others will.—I am, etc.,

Glasgow, July 20. J. W. PATTERSON.

Early Cardiac Massage

SIR,—No one will question the wisdom of Mr. Hamilton Bailey's contention that in the operating theatre at all times everything should be in readiness for the immediate application of injection into the heart and of cardiac massage should these become necessary. Some, however, will be apprehensive lest his article encourage the early use of cardiac massage in non-abdominal cases, before simpler measures have been efficiently tried. I allude especially to immediate and complete lowering of the head. Is Mr. Bailey convinced, for example, that in the case which he describes, when the patient was out of his hands at the moment of collapse, if the boy had at once been inverted and the tongue drawn forward and the chest compressed breathing and circulation would not have started again? As regards adrenaline injection has it not been generally accepted that it is the mechanical stimulus of the needle entering the auricle which is important regardless of any injection fluid?—I am, etc.,

London, July 25. J. BLOMFIELD.

Da Costa's Syndrome

SIR,—I have read Dr. Paul Wood's illuminating Goulstonian lectures (May 24 and 31 and June 7) with great interest, but there are some points to which I have to draw attention.

In discussing the mechanism of heart pain which is found in the vast majority of patients suffering from effort syndrome, Dr. Wood mentions four different theories; evidently he has overlooked the myalgia of major pectoralis, which in my experience is responsible for heart pain in the majority of cases. I described (*Brit. J. phys. Med.*, 1938, **1**, 302) the characteristic "myalgic spots" present in functional heart diseases. In 1940 (*Lancet*, **2**, 326) I described these typical myalgic spots again as simulating so-called heart neurosis, and in a case of angina of effort. The myalgic spots are constantly to be found in the origin of major pectoralis near the sternum on the left side in left mammary pain and on the right side in right mammary pain. This origin of heart pain is by no means a theory but a fact which can be verified easily. Since I have been in the Army I could confirm it again and again.

In discussing the question whether the heart pain is local or referred Dr. Wood says: "I have found no evidence in the literature relating to the effect of intramuscular novocain [i.e., injections] on referred pain." In the *Lancet* and the *Practitioner* (1941, **146**, 167) I stated most emphatically that novocain injected into a myalgic spot definitely relieves referred pain. I recommended this method not only therapeutically but also as a diagnostic test to prove conclusively that a given pain is referred. The statement, "It is well known that local intramuscular injections of novocain abolish local pain of such lesions as fibrositis," is not correct. On the contrary, in fibrositis or rheumatic myalgias referred pain only is present, and is abolished by injection into the corresponding myalgic spots.

In myalgias of rheumatic, traumatic, or idiopathic (unknown) origin patients complain of referred pain only, which does not coincide with the myalgic spots, of which they are definitely unaware. In all these cases novocain injection into the myalgic spots, not just tender spots but characterized by objective signs, relieves pain almost instantaneously and cures the disease per-

manently. Tentatively I have put forward as a working hypothesis the conception that the myalgic spots are due to a local hypoxia caused by vasoconstriction by reason of stimulation of sympathetic fibres. Since the pathological condition is situated in the muscles, one has to bear in mind the fact that adrenaline has a dual effect, causing vasoconstriction in small doses and vasodilatation in large ones (McDowall, R. J. S., *Control of the Circulation*, London, 1938, p. 268). In my opinion sympathicotonia—a hyperfunction of the sympathetic—is the cause of the effort syndrome. It is known that stimulation of the sympathetic causes a discharge of sympathin (Cannon and Rosenblueth) into the blood, which may or may not be identical with, but is most likely similar to, adrenaline.

I would like to mention here that dizziness may be caused by a myalgia of trapezius, and that breathlessness might be due to the pectoralis myalgia, since it gives rise to pain which is aggravated on breathing. In this connexion it is interesting to mention that ephedrine may produce some of the symptoms of effort syndrome, as anorexia, frequency of micturition, dry mouth, and a changed type of breathing (own experiment).

Owing to lack of space I cannot discuss the many factors which have a bearing on the function of the autonomic nervous system. There is conclusive evidence that the Ca:K ratio influences the sympathetic and parasympathetic in an antagonistic way (Zondek, S. G., *Biochem. Zschr.*, 1922, **132**, 362). It is extremely interesting that the same ratio has also a marked bearing on the tone of the capillaries—vasodilatation by Ca excess, and vasoconstriction by K excess (Sollman, T., *Manual of Pharmacology*, 1936, p. 346). In addition the blood vessels are influenced antagonistically by the local *p*H, being dilated or constricted by an acid or alkaline *p*H respectively.

Dr. Wood has conclusively shown that fear and emotional strain play a part in the effort syndrome. I fully agree with him but would like to add that these mental factors have a bearing on practically every disease, be it somatic or functional. Nevertheless one is in my opinion not justified in labelling a patient suffering from effort syndrome as psychoneurotic or hysteric. M. B. Bender (*Amer. J. Physiol.*, 1938, **121**, 609) experimenting on monkeys, suggests that during fright a discharge of a sympathetic-adrenergic and a parasympathetic-cholinergic substance takes place; hence fear and emotional strain cause a psychosomatic reaction, and not a purely mental one. Neither is it fair to label a patient suffering from "heart pain" as a psychoneurotic, since to him the pain is a real fact and cannot be talked off, even by a heart specialist's assuring him that his heart is healthy. On the other hand, extremely gratifying results are obtained by appropriate treatment of the myalgic spots. On pressure on such a spot we elicit the very pain he is suffering from ("You have got it," the patient sometimes says spontaneously), and injection of a few c.cm. of novocain solution relieves his "heart pain" easily and almost instantaneously, and permanently. This has a double effect in so far as it relieves his pain, and in doing so it convinces him to his own satisfaction that his heart is healthy, thus cutting the vicious circle so well elaborated by Dr. Wood. I am confident that these favourable results can be obtained by every physician who takes the trouble to locate the myalgic spots (not tender spots) and apply the appropriate treatment.

In conclusion I should like to say that it must be our concern to relieve a patient's justifiable complaint, instead of labelling him a psychoneurotic.—I am, etc.,

M. GOOD, M.D.,
Lieut., R.A.M.C.

June 12.

Treatment of Crush Syndrome

SIR,—In view of the high mortality among persons who have been held crushed under debris for some time, whatever treatment they have received, it seems worth while offering a simple suggestion for a line of treatment which I am told has not been tried.

It is possible that some deleterious substance derived from the injured tissues reaches the body as a whole during the time between release from pressure and commencement of treatment in hospital.

All first-aiders are keen to apply tourniquets, and, I am told, apply them in such a way as to stop venous and lymphatic return from the limb. I suggest it would be worth applying a constriction round the proximal end of a crushed limb, as soon as the limb or part of it is released from pressure, at the site of the incident before moving the patient. If sufficient skill is available, possibly a rubber Esmarch bandage applied tightly to the whole limb from above downward might be considered.

I do not presume to suggest whether the surgeon should amputate, or release the limb from pressure an inch of its length at a time, or gradually diminish the pressure on the limb as a whole.—I am, etc.,

E. CURPHEY.

Trowbridge, July 22.

Lack of Calcium

SIR,—Dr. I. Harris (July 19, p. 102) doubts that adults are suffering from lack of calcium and challenges "the authorities" to exhibit twelve patients with an "unsatisfactory condition of the bones." During the last year alone we have seen three elderly women with generalized osteoporosis complicated by collapse of a vertebral body.—We are, etc.,

GEORGE GRAHAM.
H. JACKSON BURROWS.

London, W.1, July 25.

Persistent Streptococci after Puerperal Fever

SIR,—The following case raises a point of some importance and seems worth recording.

About three weeks ago a man was admitted to hospital with a shallow ulcer about 1 inch in diameter on the ventral surface of his penis, about 1 inch behind the glans. A film from this showed a few pus cells and numerous small streptococci, and the culture was a pure growth of haemolytic streptococci which proved to belong to Group "A."

On going into the possible cause of the infection it transpired that the man's wife had puerperal fever after the birth of a child at the end of February while the patient was away from home on A.F.S. duty, from which he returned about ten days before his admission to hospital. Cultures from the wife's cervix and vagina were taken; the former yielded a pure culture of a haemolytic streptococcus, and in the latter the predominant organism was also a haemolytic streptococcus. Both these strains belong to Group "A."

The three strains were sent to Dr. S. D. Elliott of the Emergency Public Health Laboratory Service at Cambridge and he very kindly Griffith-typed them. All three belong to Type B 3264, a type recognized by Dr. Griffith as a new type which has not yet been assigned a number in the *Str. pyogenes* group.

The persistence of haemolytic streptococci in the cervix and vagina some months after an attack of puerperal fever raises the important point of the advisability of cultures being taken from all such cases to ensure that they do not become carriers. Presumably the woman would become immune to the organisms herself, but would be a potent source of infection at a later confinement.—I am, etc.,

P. LAZARUS-BARLOW.

Hastings, July 22.

The Darning of Hernias

SIR,—I was very interested to read Mr. Rodney Maingot's article (May 24, p. 777) on the floss-silk method of repair for direct inguinal hernias. Most people are agreed that catgut, being an absorbable material, is unsafe to use in the repair of a hernia. After so many days the catgut is absorbed and an undue strain may easily tear asunder the adhesions, not yet firm, left at the site of the catgut stitches. A lattice-work of an unabsorbable material inserted under no tension and forming a permanent framework on which fibrous tissue is laid down will obviously be a much safer method.

The fascia lata method of Gallie is an excellent one and gives very good results. But it entails making a long wound in the thigh and stitching the edges of fascia together after the removal of the required number of the strips, all of which add considerably to the length of the operation. There are a great number of fasciotomes on the market, but on the whole they are most tricky instruments to use. They often go wrong half-way through the operation and one is forced then to cut down; they leave a potential space in the thigh

for a haematoma; and a hernia of muscle occurs through the cut margins of the fascia lata, which can be a cause of great worry to the patient. Floss silk does quite as well as fascia lata, and, what is very important, one can use unlimited amounts, whilst one is limited to a maximum of about four strips, from each thigh, of the fascia.

About a year ago I did a radical cure on a man of 28 for a scrotal hernia *en glissade* (the size of a small football) which contained all his sigmoid colon and a great number of loops of small intestine. It was a hernia which, starting as an indirect, finished as a direct, with a neck some four inches in diameter. It would have been very difficult to do a satisfactory repair with fascia lata in that case. There would not have been enough with fascia, taken even from both thighs. Literally, I used yards of floss silk. The man has since joined the Army as A1.

The danger of a non-absorbable material is, of course, the possibility of sepsis. But if the silk is thoroughly boiled—Mr. Maingot recommends two hours—and then kept in some spirit which is washed off just before the operation, or if one uses the ampoules containing sterile floss silk as sold by John Bell and Croyden, then it is absolutely safe. It is a tragedy when a clean hernia case goes septic. Then the whole surgical ritual should be thoroughly looked into. Some months ago two of my cases in which floss silk had been used unfortunately went septic, and yet both eventually healed up completely without discharging any silk and are dry to-day, some months after leaving hospital. This shows that floss silk can cause no harmful effects, even in the presence of sepsis. I think this is greatly due to the fact that there is no chemical or other substance on the floss silk that by causing a tissue reaction and producing an outflowing of serum keeps up the discharge from the wound. So once the bacterial infection has died out the wound can heal and stay healed.

I think Mr. Maingot's suggestion of closing the crural canal from above to prevent the possibility of a femoral hernia is an excellent one. It should be reserved for direct hernias, however, when the fascia transversalis is almost non-existent. In indirect hernias it would be unwise to do this as one would have to tear through the fascia transversalis, which is after all a very important barrier to the posterior wall of the inguinal canal.

As man-power for the Services is such a vital consideration at the moment, and as hernias are so frequent in the soldier class, the choice of a satisfactory radical cure becomes a matter of national importance, especially when one remembers the reported recurrence rates—8% to 12% in the best hands. In view of this Mr. Maingot has rendered a great service in bringing up once more this question of the best method of repair of hernias, and I am sure that his floss-silk method will do a great deal in helping to lower the recurrence rate and making men fit for Army duty quicker after their hernia operation.—I am, etc.,

G. STAFFORD MAYER, F.R.C.S.,
E.M.S. Surgeon.

Herts, July 22.

Lung Collapse after Eye Operation

SIR,—I was interested in Dr. Roger Lane's case of lung collapse after eye operation (July 19, p. 86). In 1934 (*Trans. ophthalmol. Soc.*, **54**, 280) I drew attention to the occurrence of unexplained pulmonary complications after operations on the eye, the clinical picture being dullness and diminished breath sounds at one base with slight fever developing about a week after operation. As physician to Moorfields Hospital I saw many examples of this, and a smaller number of cases in which haematemesis occurred after operations on the eye in patients who had not any previous history suggesting chronic gastric or duodenal ulcer. I suggested tentatively that in both of these groups the visceral disorder might be excited reflexly by the eye operation, the afferent path being the trigeminal nerve and the efferent the vagus. The relationship between the eye and vagus function is close, as we see in the oculo-cardiac reflex and in the vomiting which often accompanies acute glaucoma.

This clinical experience recalls the perforating ulcers of the oesophagus, stomach, and duodenum which may follow experimental lesions of the hypothalamus or, rarely, operations on the brain, and which have been attributed by Cushing and others to a central disturbance of vagal innervation.—I am, etc.,

W. RUSSELL BRAIN.

London, W.1, July 25.

Treatment of Chronic Hypertensive Nephritis by Renal Extracts

SIR,—The annotation in the *Journal* of July 5 (p. 22) on the treatment of hypertension by renal extracts suggests that the case recorded below may be of interest.

A man aged 47 was admitted on October 16, 1940, to the French Hospital under the care of Dr. H. S. Stannus with old-standing chronic nephritis with hypertension; blood pressure 250/120; blood urea 160 mg. per 100 c.cm.; albumin 10 grammes per litre of urine. Marked anaemia of pernicious type and albuminuric retinitis with almost complete loss of vision in the right eye were also noted. Ordinary methods of treatment availed nothing, and a month after admission two successive attacks of acute oedema of the lungs nearly proved fatal. The blood pressure remained at 230/120; the blood urea had risen to 202 mg. per 100 c.cm.; muscular twitchings were marked, minor convulsions occurred from time to time, and mental agitation with confusion was present. At the same time almost uncontrollable vomiting was noticed and an acneform eruption (*acné urémique*) remarked.

The administration of renal extract at this point produced rather remarkable effects. Given in the first instance by rectum on account of the vomiting, it was continued by mouth as soon as the vomiting subsided, there being no preparation available for parenteral administration. Three days after the beginning of treatment vomiting ceased, followed by disappearance of the mental and nervous symptoms and lastly the cutaneous manifestations. The patient felt better and looked better; he was once again able to enjoy nourishment. The blood pressure fell to 180/100, but the blood urea continued to rise: 202 mg. per 100 c.cm. on November 18 to 250 mg. on November 23, 285 mg. on December 2, 300 mg. on December 17, 340 mg. on December 30, 360 mg. on January 7, 388 mg. on January 13, and 420 mg. on January 24, 1941, the day before death. The blood count towards the end revealed 1,500,000 red cells per c.mm. with 30% haemoglobin. Despite the mounting blood urea the patient remained pretty comfortable to the end and free of the symptoms which had troubled him before the administration of the kidney extract.—I am, etc.,

M. BENDIT.

The French Hospital, London, W.C.2, July 14.

Note by Dr. H. S. STANNUS:

The extract of kidney was used only as a last resort in an attempt to alleviate the distressing symptoms suffered by the patient. The "relief of symptoms" which occurred was quite remarkable, though probably the treatment made no difference in the course of the disease to a fatal issue. Of course, it is not certain that the amelioration in the condition was due to the extract; the constitution of the product is not even known; moreover, the value of a single observation is doubtful. On the other hand, taken as above recorded the case is not without interest as a clinical observation, always remembering the final dictum of Irvine H. Page in the Edward Gamaliel Janeway Lecture for 1941 (*J. Mt. Sinai Hosp.*, 1941, **8**, No. 1, 23): "Administration of renal extract is not yet to be considered a practical treatment."

Ether Convulsions

SIR,—May I say to Mr. Dickson Wright (July 12, p. 68), through you, that in my letter (June 21, p. 945) my first object was to describe the features of a typical ether convulsion, and that the description I gave was based upon observations made a good many years ago in a series of six or seven cases. Novocain was not used in any of them. The more recent case which I quoted for completeness (and in which ether was not given deliberately) reproduced this picture so completely that I included it as an ether convulsion. Mr. Dickson Wright tells me that it was a typical novocain convulsion. The natural inference is that the two manifestations are identical—a conclusion supported by Mr. Hamilton Bailey (July 5, p. 32), who also states the attractive hypothesis of a common toxic factor.

Mr. Hamilton Bailey also points out that by the time ether vapour reaches the patient any warmth previously imparted to it has been lost—a statement with which I agree. When I spoke of heated ether I referred to the practice of heating ether in a strong metal container in a hot-water bath to such a tempera-

ture that its vapour is driven off under considerable pressure. I believe that many analyses failed to disclose any toxic agent, and I know that a number of reported cases have occurred under open ether. Despite these facts, the evidence of my own observations points, in the absence of any more convincing evidence to the contrary, towards a toxic factor in the elaboration of which the heating of ether may play an important part.—I am, etc.,

Liverpool, July 22. CHARLES WELLS.

Treatment of Impetigo Contagiosa

SIR,—The following observations on the treatment of impetigo in Army patients may prove of value to medical officers who are now called upon to treat this class of patient.

In civil life it was my practice to use 5% sulphapyridine ointment in the treatment of this condition, and the results obtained were excellent, cure usually resulting in from three to seven days. Prior to the introduction of sulphapyridine I used the routine method of starch poultice plus lotio cupri-zincica and ung. hyd. ammon. dil., and with this about three-quarters of the cases cleared up within three weeks and the remainder after a more or less prolonged period.

During the last six months I have had occasion to treat quite a number of cases of impetigo contagiosa in soldiers. I first used 5% sulphapyridine ointment, but with very little success, no case healing up completely with its use. I then went on to "alibour" lotion and dilute ammoniated mercury ointment, and again the results were entirely unsatisfactory. The problem then presented itself as to why these two methods of treatment which were so successful in civil life failed to produce the same effect in the Army. A possible solution was suggested to me by my orderly. He observed that in Army patients any ointment will prove unsatisfactory as a therapeutic agent, owing to the fact that the comparatively high-collared tunics have rubbed off the ointment in a very short time and the collar becomes a dirty greasy mess on which no doubt the streptococcus of impetigo finds a good place to incubate and which acts as a focus for the continued spread of the disease.

On active service it would be a considerable nuisance if soldiers suffering from such a mild illness as impetigo had to either go without their tunics or have their face covered with any form of dressing during the day. It was therefore decided to try the effects of an antiseptic lotion alone, and we chose the old-fashioned 1 in 1,000 corrosive sublimate because it was cheap, easily obtained, and sufficiently easy to make up for any unqualified dispenser. This has proved a very satisfactory method of treatment. The lotion is dabbed on three times daily, the man shaves every third day and has his razor and brush sterilized by the orderly in the medical inspection room immediately after shaving. The face is uncovered during the day, but an aseptic dressing is put on at night to prevent spread by means of the pillow. By this method it has been found possible to cure most cases of impetigo in Army patients within ten days.—I am, etc.,

July 21. E. SNELL, Lieut., R.A.M.C.

Chronic Sick

SIR,—Very reluctantly I ask you to publish one more letter from myself on the subject of the "chronic sick." I say reluctantly because a week ago I had quite made up my mind that the "chronic sick" had very few friends either in the Ministry of Health, among medical members of Parliament (with the striking exception of Sir E. Graham-Little), or in the medical profession generally, and therefore it was a mere waste of time pursuing the subject any further.

In your issue of July 19 (p. 100), however, there appears a long letter from Dr. Leonard G. Parsons upon which I should like to make several brief observations. The main body of the letter is devoted to various comments and criticisms of a letter in the *Journal* of June 28 (p. 987) from "De Senectute." I am not concerned to defend "De Senectute"; no doubt, whoever he is, he can look after himself. But I am concerned with those parts of Dr. Parsons's letter which refer (*a*) to the occupation of beds by the evacuated chronic sick which were "provided for acute and Service sick and air-raid casualties," and (*b*) to the nursing of the chronic sick by "members of the C.N.R., Red Cross, and Order of St. John," as well as his suggestion that auxiliary hospitals are unsuitable for the care of the chronic sick.

With regard to (*a*) the comment I wish to make is that this is only another example of the incompetence and unpreparedness of the Ministry of Health in all matters concerning the measures which should have been taken long before war broke out to provide suitable accommodation in the less vulnerable areas not only for the chronic sick but for many other types of evacuees. Ordinary common sense, foresight, and prudence, which should have characterized the work of the Ministry of Health, were simply not there. If they had been it would not have been necessary to take "panic measures" a year or more after war broke out to provide suitable accommodation outside our great industrial towns for evacuees of all kinds, including the "chronic sick," aged and infirm, and young children. But what happened was that those who were then responsible for the policy of the Ministry were so obsessed with the notion that the only thing they had to think about was hospital accommodation for "30,000 casualties per day" in London alone that the staff concerned could think of nothing else. In these circumstances it is easy to understand how it came about that when "chronic sick" patients were being killed in their beds in large public institutions in London and elsewhere by direct bombing the Ministry adopted the usual "panic measures" and rushed patients of this kind off to hospitals in the less vulnerable areas, where beds had been set aside for the acute sick, casualties, etc.

With regard to (*b*) I do not agree with Dr. Parsons that auxiliary hospitals are unsuitable for the chronic sick. At least that is not my own experience. I have seen a good many auxiliary hospitals which would be eminently suitable; but I do not suggest that all of them are, for the simple reason that I have not seen them. On the other hand, there are nearly 200 auxiliary hospitals in England and Wales, with a total accommodation of nearly 12,000, and most of them are empty and likely to remain so; if properly used I do not see why there should be any practical difficulty over the staff question. No one with any knowledge of the skill and patience and tact required to nurse the "chronic sick" would for one moment suggest that they should be nursed by V.A.D.s, etc. The obvious course to adopt is to transfer the medical, nursing, and all other staff who have been looking after the "chronic sick" to the new accommodation whenever provided, and I am unable to understand why this course should not be adopted as part of the scheme of transfer. It is quite true that the work could not be undertaken by the Joint War Organization of the B.R.C.S. and Order of St. John. It is obviously unsuitable work for such a voluntary body. What would be required would be simply that the Joint War Organization and the Ministry of Health should agree that certain of the existing auxiliary hospitals should be transferred for the duration of the war to the local public health or local public assistance authority for the special purpose of providing for the "chronic sick." I do not say that such a step would solve the problem, but it would go a long way towards it.—I am, etc.,

Criccieth, July 19. FREDERICK MENZIES.

Physical Medicine and Orthopaedics

SIR,—Now that all your correspondents seem to have said their say about the practitioners in physical medicine and their art and science, may I, as one of the elder of the genus in this country—save, of course, for the Spa practitioners—wind up with a few notes.

First, let me say how gratifying it has been to watch the interest that your original annotation has evoked. Thirty years ago the correspondence which followed would have been unthinkable, so few would have been the numbers of those with adequate knowledge to write. Even our critics have shown the importance they attach to our activities.

With regard to status, all that need be said is that our art is, or should be, the handmaid of the profession as a whole. Few indeed can be the number of our fellow practitioners who, had they adequate knowledge, could claim that the art of physical therapy could find no useful place in the treatment of their patients during some stage of illness and disability or during convalescence therefrom. Obviously, therefore, the term

"orthopaedic physician" is a poor, inadequate description for us. The orthopaedic surgeon may, it is true, find that—*pace* Böhler—physical therapy is applicable to the vast majority of his cases with advantage; not infrequently without it his surgery would be useless. This is the reason why most of them study the elements of physical therapy, but mere acquaintance with those elements does not fit them to prescribe all that is best in physical therapy for their patients. We hold, as a standard of efficiency, that we cannot honestly prescribe any treatment which, without aid, we are unable to perform for ourselves at least as efficiently as those to whom the work is entrusted. Otherwise how can we prescribe with accuracy and precision, or judge by results whether progress is the best obtainable? If barely acquainted with the elements, how then can orthopaedic surgeons demonstrate technique to the masseur or masseuse, or judge of the finesse of technique? The physician or surgeon, orthopaedic or otherwise, who relies on his knowledge, or often lack of it, even in regard to what can only be termed by us as the "beggarly elements," cannot expect the best of treatment for his patients, or grumble if they, in despair, seek ultimate relief from adequate physical medicine.

Staff status is another story—no one can expect election to staff rank by his colleagues till he has proved his worth and, perhaps more important, his ability to co-operate with them. It is granted readily enough when this has been done, and what more can we ask or expect? We are getting on. A very few years ago no practitioner of physical medicine had been elected to the Fellowship of the Royal College of Physicians; now there are five at least.

Finally, may I pay tribute to the members of that magnificent body the Chartered Society of Massage and Medical Gymnastics for the part they have played in the advancement of physical therapy? When I first became acquainted with their activities in 1907 there were some 700-odd members; now there are 12,814—surely a striking testimony to their usefulness and efficiency. Without their aid and loyalty to our profession physical therapy could not have known the yearly advance in technique which takes place, nor could the practitioners of physical medicine have advanced in numbers, knowledge, and experience to the extent that has in fact occurred.

There is, however, one outstanding weakness in physical medicine which must be overcome before it finally comes into its own. This is that there is no general standard of knowledge required of us in all the different branches of our art to merit our designation as practitioners of physical medicine. There is as yet no course of training available which fully covers the whole field. Hence some of us are experts in hydrotherapy, others are mainly electrotherapists, while yet others are more skilled in actinotherapy or in manipulative treatment, be it of soft parts or of joints. Expert knowledge of all branches of our art cannot be expected of all of us as yet, and before the art can be attained the science is essential. Some day in the near future this deficiency will be remedied. Even as we are we can be of service; in the future we shall be more so; and meanwhile, if some of our medical colleagues find no use for us, the general public continues to do so and to insist on their advisers co-operating with us.—I am, etc.,

London, N.W.1, July 20. JAMES MENNELL.

*** This correspondence is now closed.—ED., *B.M.J.*

Medical Planning

SIR,—In the *Journal* of June 21 (p. 942) it is reported that the president of the Faculty of Radiologists, Dr. Cochrane Shanks, referring at the annual meeting of the Faculty to his position as the Faculty's delegate to the B.M.A. Planning Commission, promised to send a questionary among the members of the Faculty asking them, under seal of anonymity, to give such facts about their work as they felt disposed to divulge; also to give him their views on what alterations and improvements were called for in the radiological services of the district. This step is undoubtedly to be welcomed and recommended to other members of the Planning Commission, particularly if they would couple it with a declaration that no action would be taken until a policy had received sanction of a fully informed medical profession.

Doubtless certain of the apprehension given to the Planning Committee arises from the fact that it is by no means unknown for an inadequately informed public to be committed by virtually self-elected bodies to policies which may produce results entirely different from those desired by the majority. What has happened not once but many times may well happen again. Without intending to criticize any member of the Commission either directly or indirectly in their voluntary acceptance of a task, onerous, difficult, and likely to be thankless, it is permissible to ask for it to be made known to those who are directly concerned how selection of this committee was brought about or what arrangements will be made to secure full representation of every member of the profession.

A large number of doctors to whom I have spoken have a viewpoint best described as "apprehensive" of the outcome of all this planning, but unfortunately almost invariably coupled with it is a feeling of hopeless resignation. They are not prepared to do anything to alter their future, let alone take the time and trouble necessary to seek causes for a state of affairs which they regard as becoming extremely unpleasant. A review of the letters over the past few months in the *Journal* shows that the greater number fluctuate between the Scylla of an "improved" panel system and the Charybdis of undefined State Medical Service. Is this not the unmistakable result of the organized propaganda and subtle distortion of fact which tries to make it appear that the only alternative to-day facing the British peoples is military domination by Nazism or a generation of vicious and intolerable taxation in an impossible attempt to pay a second or a third time or even more for a war which then will have been paid for in "blood, toil, tears, and sweat"?

It is this perfect parallel with world affairs which makes it a certain prediction that no satisfactory outcome can arise from the activities of the Planning Commission unless a revolution in public thought and action causes the complete subjection of those responsible for a policy which over the past fifty years has been gathering control of personal initiative to its own keeping, planning to assign the national and individual sovereignty of this people to a completely centralized and world-dominating economic federation. The facts are beyond all disproving and the conclusions arresting. I venture to predict that a mass of evidence could be placed before the Medical Planning Commission proving the urgent need of the moment is not detailed Utopian planning for the future of medicine but an active awakening of democratic control and a bonding of medical opinion with a policy based on an undistorted conception of realities.

The doctor cannot control the policy of his institutions if they are too large, nor can he direct their successful functioning if they remain dependent on the arbitrary grants by centralized interests of the financial credit necessary for them to carry out their work. Control of policy has been steadily taken from the doctor. Faced with a deliberately produced diminution of private practice and an extending panel system or State service, the real result is a restriction of personal initiative. A policy of such nature does not exist by chance and must be reversed if existence is to be tolerable.

The best work the Planning Commission could do would be to awaken the members of the medical profession to the truth that their future depends on their own efforts to secure in every sphere a policy which unites personal responsibility with power; which everywhere matches physical ability to produce results needed with financial ability to do it—policies which dispense with bureaucracy and "red tape." Then we can build a future worthy of our heritage.—I am, etc.,

Belfast. DOUGLAS BOYD, M.B., D.M.R.E.

The report for 1940 of the St. John Ophthalmic Hospital, Jerusalem, shows that work, despite war conditions, was heavier than ever. In-patients numbered 926, an increase of 234 over the previous year, and the total attendances in the out-patient department numbered 119,986, which constitutes a record for the hospital, and new out-patients were 21,252. The work on the new south block has been proceeding satisfactorily. The Order of St. John has offered it to the Government of Palestine for the duration of the war to be used as a civilian casualty hospital, and the offer has been gratefully accepted.

Obituary

SIR WILLIAM WILLCOX

Dr. J. D. Rolleston writes:

Beyond the statement that he served on a special committee at headquarters on tests for drunkenness the otherwise excellent obituary of Sir William Willcox in the *Journal* of July 19 (p. 103) contains nothing to indicate the interest which, without being an abstainer, he always took in the alcohol problem. In particular no mention is made of his connexion with the Society for the Study of Inebriety, of which he was president from 1924 to 1927. In 1923 he delivered the Norman Kerr lecture before this society, his subject being drug addiction, and in 1924 his presidential address was devoted to the aims and work of the society. He also always took an active part in the discussions held at the society's meetings. Furthermore he contributed an article on the medical aspects of temperance to a book entitled *Confirming the Facts*, recently published by the Temperance Collegiate Association, and containing articles by Sir Frederick Gowland Hopkins, Prof. Amy M. Fleming, Mr. W. McAdam Eccles, Lord Stamp, Sir Leonard Rogers, and others.

Early this year the liner on which Dr. HILDA CRICHTON BOWSER was returning to India was shelled in mid-ocean by a German surface raider. Most of the lifeboats were thus damaged and fellow passengers have reported that Dr. Bowser was in one which had been seen to sink. The more seaworthy boats were too full to rescue survivors, who had to be left in the water in the hope that they would be picked up by a boat which had been launched from the raider. This hope has proved vain, and the Baptist Missionary Society and a wide circle of friends now mourn the loss of the Society's senior medical missionary in India. Dr. Bowser was the daughter of the late Principal of the Midland Baptist College. She took her B.Sc. degree from Nottingham University College before entering the London School of Medicine for Women, where she qualified M.R.C.S., L.R.C.P. in 1919 and later took the M.B., B.S. of London University. Relinquishing her studies for the degree of M.D. in obstetrics she sailed in 1923 to India, and for eighteen years built up a unique hospital and nurses' training work at the Rahmatpur Women's Hospital at Palwal in the South Punjab. Her reputation and influence were felt in a wider circle in India. She represented the Association of Medical Women on the governing board of the Lady Hardinge Medical College in Delhi, and acted as chairman of the North India Board for Nurses' Examinations. She maintained the highest standards of professional work, and the reports of Government inspectors invariably praised the efficiency of what was considered as a model rural hospital. Physically robust—a college and county hockey captain—and possessing great mental vigour, Dr. Bowser was the embodiment of the ideal of "mens sana in corpore sano." Her gifts and graces were wholly dedicated to a life of service. It is men and women like Hilda Bowser who are responsible for the fact that the phrase "missionary spirit" has found a place in the vernacular of a country which needs and greatly admires the spirit of the Good Physician.

We regret to announce the death after a long illness, on June 13 at the age of 74, of Hofrat Professor JULIUS ZAPPERT of Vienna at Slough, where he had been living in exile for the last two years. His chief work was concerned with the neurology of children, his principal publications being devoted to Heine-Medin's disease (1911), diseases of the nervous system in childhood (1922), convulsions in childhood (1928), and post-vaccinial encephalitis in conjunction with Dr. Marius Kaiser which received notice in this *Journal* (1939, **1**, 59).

The following practitioners have died abroad: Dr. LARS WILHELM FAGERLUND, a Finnish anatomist and epidemiologist, author of numerous works, especially on medical jurisprudence, leprosy, and tuberculosis, aged 87; Dr. JOHANNES WILHELM HJELMMAN, a Helsingfors dermatologist and syphilologist, aged 79; and Dr. LLOYD VERNON BRIGGS, past president of the New England Society of Psychiatry and former director of the Massachusetts Society of Mental Hygiene, aged 77.

Universities and Colleges

UNIVERSITY OF OXFORD

The first examination in Special and Clinical Pathology begins on September 30, and names must be received at the University Registry by 3 p.m. on Wednesday, September 10. The attention of candidates is drawn to the facts that: (1) Certificates 4 and 10*b* must be produced. The former is to the effect that the candidate has been instructed in special pathology, including post-mortem examinations, and clinical pathology for a period of not less than eighteen months. The latter is to the effect that the candidate has completed twenty-one months of systematic clinical instruction. (2) They must also offer forensic medicine and public health unless they have already passed in it.

UNIVERSITY OF LONDON

The Principal's Report

The report of the Principal, Mr. H. L. Eason, on the work of the University during the year 1940-1 has now been printed, and much of it is naturally concerned with the war and its effects upon academic life in general, on teaching and research, and on the buildings of the university and its constituent schools. In his introduction Mr. Eason notes that the results of intensive air raids on London have fully justified the policy of dispersal generally adopted in the summer of 1939. The damage to university buildings has been so severe and so widespread that if the schools had still been in London the work of the internal side of the university would have practically come to an end for the time being. University College has suffered very badly, and one of the more recent sufferers is the London School of Hygiene. The hospitals attached to the medical schools of the university have almost without exception been severely damaged, but owing to the decentralization of staffs, students, and patients under the Emergency Medical Service, medical education has been maintained at a high level. The greatest sufferers among the medical schools have been St. Bartholomew's and the London School of Medicine for Women. Notwithstanding all the handicaps under which it has laboured, by reason of war damage, decentralization, and delays and difficulties due to disturbance of communications, the work of the university has been well maintained, and normal examinations have been held, though in some cases in provincial centres. The Principal conveys the grateful thanks of the University of London to all those provincial universities and university colleges which have hospitably entertained staff and students and enabled the examinations to be carried on without material loss of efficiency. Among many miscellaneous items mentioned in this report are the foundation by Dr. T. H. Sanderson-Wells of prizes in the pathology and physiology of food, and funds for an occasional lecture on human ailments with special reference to soil fertility; the appointment of Dr. J. H. Gray to the chair of anatomy at St. Mary's on the retirement of Prof. J. E. S. Fraser; and special work of therapeutic value developed in connexion with the military and E.M.S. hospitals. In conclusion Mr. Eason writes: "This report necessarily deals in a scattered way with a scattered university. While exile has its disadvantages both for staff and students, it has its advantages in stimulating adaptability to circumstances and in providing an education in its methods, habits, and customs of universities other than one's own. Our students and teachers have certainly not sat down by the waters of Babylon and wept."

GUY'S HOSPITAL MEDICAL SCHOOL

The following awards have been made for 1941: *Entrance Scholarship in Arts* (*value £100*): E. L. W. Leiser. *Entrance Scholarship in Science* (*value £100*): Divided between J. C. Crook and D. D. Hilton.

UNIVERSITY OF EDINBURGH

A graduation ceremony was held on July 16, when the following degrees and diplomas were conferred:

M.D.—[2]D. S. Fairweather J. A. Farfor, Captain, R.A.M.C., [1]C. A. Green, [1]D. Harley, A. G. MacGillivray, [3]H. Miller, Surgeon Lieutenant, R.N.V.R., A. Paterson, A. I. Ross, [2 3] W. S. Thomson, Lieutenant, R.A.M.C.

PH.D.—A. E. Sundareson, M.B., B.S.

M.B., CH.B.—P. A. Adam, R. S. F. Adam, W. J. Aitken, F. G. Alexander, W. G. Alexander, A. Anderson, W. Anderson, Winifred A. Bailey, Helen S. Barrett, C. L. Bikitsha, E. C. B. Bramwell, A. S. Brown, I. G. Brown, J. B. Brown, M. L. Brown, R. Brown, Maud L. Buchanan, G. M. Carstairs, Josephine A. Cartwright,

T. M. Chalmers, Edith M. Churchward E. A. Claireaux, J. R. Clark, L. E. S. Coghlan, O. C. Colt, J. F. Cowan, J. D. Crombie, Rosina G. Dabb, A. B. da Costa, W. J. E. Darling, Esther A. Davidson, F. B. Davidson, J. Davidson, J. R. Deuchars, H. S. Dewar, J. S. Drummond, J. W. Drummond, A. D. Drysdale, E. C. Eadie, Ethel F. Edwards, A. W. G. Elliott, Esther T. Ewing, E. C. Field, D. E. P. Forbes, W. R. Fyvie, T. M'L. Galloway, M. Gandz, [4]J. A. L. Gilbert, I. C. Godfrey, J. M. Gold, I. W. B. Grant, Marie P. S. Grant, A. A. Guild, D. S. Harling, Elizabeth G. Harris, K. W. Horn, H. Hutchison, Katherine I. Izat, D. Jaboor, P. M. Kerr, A. M. Langwill, [4]J. R. Lauckner, J. Lawson, P. B. Lockhart, Philippa M. Ludlam, J. M. M'Alpin, J. M'Clemont, R. N. C. M'Curdy, H. MacL. T. MacDonald, J. A. Macfarlane, R. C. M'Laren, I. MacC. MacLeod, G. C. Malloch, K. L. Marks, Margaret St. C. Masson, Ellis M. Matthew, F. G. Maxwell-Smith, J. C. G. Mercer, A. M. Merriweather, Grace M. Mitchell, R. C. E. Moffat, [4]A. G. C. Neill, D. F. Nicholson, J. Orr. C. A. Palfrey, R. B. Parker, W. H. Parkinson, J. M'D. Paterson, M. G. Pearson, H. J. Powell, J. W. T. Pretsell, T. Primrose, V. T. Pugh, B. C. E. Richardson, M. R. Rifaat, Winifred B. Ritchie, W. G. Robertson, H. E. Robins, H. N. Robson, J. D. Ross, [4]J. Y. W. Russell, A. J. Sangster, [4]Sheila P. V. Sherlock, O. H. Siung, Betty V. Slesser, J. D. A. M. Smart, A. C. Smith, C. J. C. Smith, Margaret Sinclair Smith, Margaret Steele Smith, J. C. W. Somerville, J. J. Stevenson, N. R. Stewart, J. R. Stuart, A. P. Tait, Helena P. M'I. Taylor, Mildred S. Tie-Ten-Quee, T. Tie-Ten-Quee, J. E. Tinne, W. H. Toms, Janet C. Trotter, Davina M. van Weel, J. W. Walford, Margaret J. P. Walker, Grizel Warnock, Elizabeth M. Watson, W. B. Whiston, J. G. Whitty, J. Wilkinson, Jean C. Willison, J. A. C. Wilson, Sara S. Wood, H. C. Worrall, Kathleen M. F. Worrall (*née* Whalley), R. K. W. Yang, W. W. Yellowlees.

D.P.H.—Olive B. Barnetson, [5]G. A. R. Brown, [5]W. D. Buchanan, [5]J. Cameron, Monica de S. Craig, [5]W. Giles, Rachel Hunter, [5]R. P. Seymour, [5]Mora A. Smeaton, Mona M. M'F. Thomson.

DIPLOMA IN MEDICAL RADIOLOGY.—[5]K. Brauer, [5]B. Donnelly, G. H. Illingworth, [5]J. A. Wain.

[1] Awarded gold medal for thesis. [2] Highly commended for thesis. [3] Commended for thesis. [4] Passed with honours. [5] *In absentia.*

The following prizes were presented:

Maclagan Prizes in Forensic Medicine: D. Henderson and R. T. S. Louttit. *Straits Settlements Gold Medal:* W.-f. E. Baumann. *Ettles Scholarship and Leslie Medal, Scottish Association for Medical Education of Women Prize, Mouat Scholarship in the Practice of Physic, Dorothy Gilfillan Memorial Prize, Beaney Prize in Anatomy and Surgery, Keith Memorial Prize in Systematic Surgery, and Murdoch Brown Medal in Clinical Medicine*: Sheila P. V. Sherlock. *Buchanan Scholarship in Midwifery and Gynaecology and Annandale Medal in Clinical Surgery:* Josephine A. Cartwright. *James Scott Scholarship in Midwifery and Gynaecology and Royal Victoria Hospital Tuberculosis Trust Medal:* J. Y. W. Russell. *Conan Doyle Prize:* W. R. Fyvie. *Wightman Prize in Clinical Medicine:* A. M. Merriweather. *Pattison Prize in Clinical Surgery and Thomson Memorial Medal in Child Life and Health:* J. A. L. Gilbert. *Sir Humphry Rolleston Prize:* J. Orr. *Murchison Memorial Scholarship in Clinical Medicine:* A. A. Guild. *Ellis Prize in Physiology:* A. E. Ritchie. *Gunning Victoria Jubilee Prize in Chemistry:* G. T. Meiklejohn. *Gunning Victoria Jubilee Prize in Materia Medica:* G. A. Levvy. *Gunning Victoria Jubilee Prize in Medicine:* J. Innes. *Lewis Cameron Undergraduate Prize in Bacteriology:* B. Cruickshank. *Biggam Medal and Prize in Pathology:* H. T. G. Strawbridge. *Cunningham Memorial Medal and Prize in Anatomy:* P. R. Walbaum. *Whiteside Bruce Bursary:* A. D. Bethune and Constance C. Forsyth (equal). *Vans Dunlop Prize in Botany and Zoology:* Constance C. Forsyth and Hilary F. H. Hamilton (equal).

POLISH SCHOOL OF MEDICINE AT EDINBURGH

The degrees of M.B., B.Ch. were conferred on K. Bazarnik, Lieutenant-Pilot, Polish Air Force.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the Royal College of Surgeons of Edinburgh held on July 21, with Dr. H. M. Traquair, President, in the chair, the following, who had passed the requisite examinations, were admitted Fellows:

F. P. Cameron, Lyra M. de Souza, K. Fraser, J. W. Frost, W. J. F. Guild, Ethna W. Little, G. E. Moloney, D. M. Morrissey, K. D. Rao, E. W. Somerville, B. G. Spiers, W. S. Tulloch.

CONJOINT BOARD IN SCOTLAND

The following candidates, having passed the final examinations, have been granted the diploma of L.R.C.P.Ed., L.R.C.S.Ed., and L.R.F.P.&S.Glasg.:

N. V. Appavoo, H. K. Banda, F. H. Batchellor, S. J. Blau, A. H. Brambir, W. Brown, M. Burdman, D. Davidson, W. J. Dempster, H. H. Feldman, W. J. E. Fernando, J. Fitzsimons, S. Gelband, E. G. Gordon, H. P. Hall, H. V. Hankins, A. S. B. Hebron, M. H. Hurwitz, J. Ireland, L. Kaywin, H. Laret, M. Links, E. Lipschik, M. K. McCabe, A. McCall, T. McMurray, J. C. MacWilliam, I. Markowitz, H. Pearl, J. M. Stewart, L. J. Swirsky.

E. Nobel, a graduate of a recognized foreign university, was also admitted a Licentiate.

The Services

DIRECTOR-GENERAL, ARMY MEDICAL SERVICES

Colonel (Temporary Brigadier) Alexander Hood, C.B.E., has been appointed Director-General, Army Medical Services, in succession to Lieutenant-General Sir William P. Macarthur, K.C.B., D.S.O., O.B.E., who retired on August 1.

The new Director-General graduated in medicine at Edinburgh University in 1910 and took the M.D. degree in 1931. He entered the R.A.M.C. in 1912 after serving as house-surgeon at the Edinburgh Royal Infirmary. He has been D.D.M.S. in France and D.D.G. at the War Office.

HONORARY SURGEONS TO THE KING

Surgeon Rear-Admiral G. F. Syms, R.N., has been appointed an Honorary Surgeon to the King.

Colonels T. C. Boyd, V.H.S., and H. J. M. Cursetjee, D.S.O., V.H.S., I.M.S., have been appointed Honorary Surgeons to the King, vice Colonel J. Taylor, C.I.E., D.S.O., I.M.S. (ret.), and Major-General N. M. Wilson, C.I.E., O.B.E., I.M.S. (ret.), respectively.

ARMY AWARDS

Major F. McL. Richardson, R.A.M.C., has been awarded the D.S.O. and has been mentioned in dispatches, and Captains H. S. Ahluwalia and M. C. L. Smith, I.M.S., have been awarded the M.C. in recognition of gallant and distinguished services in the Middle East.

MENTIONS IN DISPATCHES

Surgeon Lieut. John Ffrangcon Roberts, R.N.V.R. (H.M.S. *Rosaura*) has been posthumously mentioned in dispatches for gallantry in saving a wounded shipmate.

COMMENDATION

Lieut. Frederick Graham Millar, R.A.M.C., has been commended for brave conduct.

CASUALTIES IN THE MEDICAL SERVICES

ROYAL ARMY MEDICAL CORPS

Lieut. ANTHONY JAMES MOON, who was reported missing in s.s. *Lancastria* in June, 1940, is now presumed killed. He qualified M.R.C.S., L.R.C.P. in 1936, and took the degrees of M.B., B.Chir. of the University of Cambridge in the following year. Before the war he was in practice at Wallington, Surrey.

War Substantive Captain ROBERT MONTGOMERY MAXWELL, who has died of wounds, received his professional education at the University of Glasgow, where he graduated M.B., Ch.B. in 1936. His home was in Glasgow.

Prisoners of War

Captain Alfred Ruff Darlow.
War Substantive Captain Harry Acroyd Barker.
Lieut. James Alexander Savage Mulligan.

DEATHS IN THE SERVICES

Major-General Sir OWEN EDWARD PENNEFATHER LLOYD, V.C., K.C.B., late R.A.M.C., died at St. Leonards-on-Sea on July 5, aged 87. He was born on January 1, 1854, the son of Major M. P. Lloyd of the 58th Foot and of Co. Roscommon, was educated at Fermoy College, at the Queen's University, Cork, and in the school of the Edinburgh College of Surgeons, taking the L.R.C.P.&S.Ed. in 1877. He entered the Army as surgeon in 1878, became full colonel in 1905, surgeon-general in 1909, and retired in January, 1914, but rejoined as soon as war broke out in August, 1914, and served as D.M.S. of the Southern Command. He won the V.C. in the Kachin, Burma, expedition of 1892-3, received the C.B. in 1910, and was promoted to K.C.B. in 1919. From 1922 to 1924 he was a colonel commandant of the R.A.M.C. During his first year of service he took part in the Zulu War of 1879-81, and was present at the storm and capture of Sekukunni's stronghold, receiving the medal and clasp. In the first Boer War of 1880-1 he formed one of the garrison of Standerton, which held out against a superior force of Boers till the end of the war. During the Burmese War in 1892-3 he won the V.C. for his share in the defence of the Siva post in the Kachin Hills. The announcement in the *London Gazette* read as follows: "During the attack on the Siva post by Kachins on January 6, 1893, Surgeon-Major Lloyd, on hearing that the C.O., Captain Morton (who

had left the fort to visit a picket about 80 yards distant), was wounded, at once ran out to his assistance under a close and heavy fire, accompanied by Subadar Singh. On reaching the wounded officer, Surgeon-Major Lloyd sent Subadar Singh back for further assistance, and remained with Captain Morton till the Subadar returned with five men of the Magwe Battalion of Military Police, when he assisted in carrying Captain Morton back to the fort, where that officer died a few minutes afterwards. The enemy were within 10 or 15 paces, keeping up a heavy fire, which killed three men of the picket and also Bugler Purna Singh. This man accompanied Captain Morton from the fort, showed great gallantry in supporting him in his arms when wounded, and was shot while helping to carry him back to the fort. The native officer and five sepoys above alluded to have been awarded the [Indian] Order of Merit." After Captain Morton's death Surgeon-Major Lloyd took command of the fort and brought the fight to a successful issue. He served afterwards as medical officer to the Franco-British Boundary Commission on the Mekong River in 1894-5, and in the same capacity on the British-Chinese Boundary Commission on the Burmese frontier in 1898-9, acting for a time as commissioner in the place of Sir George Scott. On his return to England he served as senior medical officer of the Dover Garrison and District. In 1905 he returned to India as principal medical officer of the Bareilly Brigades, when he was appointed Honorary Surgeon to the Viceroy. Subsequently he served for a short time as principal medical officer in South Africa. He had been a member of the British Medical Association for twenty-two years.

Major-General Sir WILLIAM WATSON PIKE, K.C.M.G., D.S.O., R.A.M.C. (ret.), died at Lincoln on June 26, aged 81. He was born in Co. Mayo on March 10, 1860, the son of the late Mr. W. Pike of Glendaray, and was educated at Dublin, taking the L.R.C.P. and S.I. in 1880 and the F.R.C.S.I. in 1888. In his student days he was a famous rugby international, playing at three-quarter back in the Irish team on several occasions. He entered the Army as surgeon in 1882, reached the rank of full colonel in 1911, was specially promoted to surgeon-general for distinguished war services in 1917, and retired in 1920. He served throughout the South African War of 1899-1902, when he took part in the relief of Kimberley; in operations in the Orange Free State, including the actions of Paardeberg, Poplar Grove, and Dreifontein; in the Transvaal, including actions at Pretoria; and in Cape Colony; was twice mentioned in dispatches and received the Queen's medal with five clasps, the King's medal with two clasps, and the D.S.O. In the war of 1914-18 he served first as A.D.M.S. of a division, then as D.D.M.S. of a corps, but in 1917 as D.M.S. of the Fourth Army. He was then sent to East Africa to confer with General Smuts on the medical organization of the troops in that theatre of war. In 1918-19 he was serving in India on special duty and on his return home was made a K.C.M.G. Before receiving this honour he was mentioned in dispatches three times and received the C.M.G. as well as a special promotion. Sir William Pike had been a member of the British Medical Association for thirty-five years. In 1886 he married Sara Louisa, daughter of Mr. E. Wheatley; she died in 1918, leaving a daughter who married Colonel O. Y. Hibbert, and died in 1935.

Lieutenant-Colonel DAVIS HERON, C.I.E., I.M.S. (ret.), died suddenly at Ashridge Hospital on June 24, aged 63. He was born in January, 1878, and was educated at the University of Edinburgh, where he graduated M.B., Ch.B. in 1900. He took the F.R.C.S.Ed. in 1912. After filling the post of house-surgeon at Scarborough Hospital and Dispensary and serving as a civil surgeon in the R.A.M.C. in 1901-2, entered the I.M.S. in 1903, became lieutenant-colonel in 1922, and retired in 1930. He served during the war of 1914-18, was mentioned in dispatches in 1917, and received the C.I.E. in 1918. He had been a member of the British Medical Association for thirty-five years. He leaves a widow.

On production of a certificate from the doctor or midwife who has been booked to attend a confinement, or, in the case of a woman attending an ante-natal clinic, from the medical officer of health, expectant mothers will be supplied by welfare authorities with fifty coupons to buy materials for garments, which should be made before the baby is born. The certificate, which should be given as soon as the diagnosis is made (usually the sixth month of pregnancy), should state the mother's name and address, her National Registration number, and the approximate date on which the confinement is expected. Double the number of coupons will be issued where a positive diagnosis of twins has been made and confirmed.

Medical Notes in Parliament

In the House of Lords on July 22 the Royal Assent was given to the Finance Act. In the House of Commons on the same day the National Health Insurance, Contributory Pensions, and Workmen's Compensation Bill passed its remaining stages.

Pharmacy and Medicines Bill

The House of Commons in Committee amended the Pharmacy and Medicines Bill on July 15 and 16.

On Clause 3 (Prohibition of advertisements relating to certain diseases) Mr. PETERS moved to add to the list of those to whom prohibited advertisements might be sent persons who, although not registered practitioners, were engaged in medical research. Mr. ERNEST BROWN said the clause was a fundamental one to prevent sufferers and their relatives being imposed on by advertisements of useless remedies. The amendment was too vague. He would be glad to discuss with Mr. Peters any proposal affecting a definable group. The amendment was withdrawn.

Dr. RUSSELL THOMAS criticized the list of diseases cures of which were not to be advertised. He said the number of people suffering from locomotor ataxy was so small that it would not pay to advertise cures for it. There was nothing to prevent the patient taking advertised cures for neuritis and dizziness for years till this disease was diagnosed. Similarly persons suffering from diabetes used all sorts of patent remedies for their weakness until their disease was diagnosed. The clause would have no effect on the advertising campaign for debility and weakness. The inclusion of glaucoma was futile. No vendor of patent medicines would say he had a cure for cataract or glaucoma, but there would be ample scope for the patent medicine vendor to advertise remedies for the symptoms. In the case of Bright's disease there was every field before the disease was diagnosed for the vendors of patent medicines to sell wares for the treatment of slowly developing symptoms. Tht inclusion of Bright's disease would have no effect on the patent medicine trade. The same thing applied to epilepsy and paralysis.

Miss HORSBRUGH said the clause would make illegal the advertising of specific articles as cures for particular diseases, not the treatment of those diseases. Proceedings would not be taken except with the consent of the Attorney-General or Solicitor-General.

DISCLOSURE OF INGREDIENTS

Mr. JAMES GRIFFITHS moved to provide that the disclosure must be in English. Dr. RUSSELL THOMAS said a famous pill whose composition in Latin would read something like: "Sap. moll., ext. aloin, zingiberis" would probably not flourish so much if on the wrapper in plain English were written: "Soap, aloes, and ginger." Mr. BROWN said disclosure should be made in terms clearest to those who had scientific knowledge and to those who bought. He had an amendment to leave out "composition" and to insert "accepted scientific name or other name descriptive of the true nature." He would go into the matter again before the Report stage. Mr. James Griffiths then withdrew the proposal that disclosure must be in English, and the House accepted Mr. Brown's amendment.

The House negatived an amendment, proposed by Sir THOMAS MOORE on behalf of the Society of Herbalists, which would exempt from detailed disclosure a remedy composed of a non-poisonous plant or plants.

On the motion of Captain ELLISTON the coming into force of the Act was delayed from January, 1942, to July, 1942, to give a sufficient period for disposal of stocks.

On Clause 9 (Repeal of medicine duties) Sir FRANCIS FREMANTLE said his friends agreed to this clause only if other conditions were laid down for complete and effective control of advertisements and the disclosure of ingredients. When the Purchase Tax was removed there would be a case for resuming the taxation of medicines.

ENFORCEMENT OF THE BILL

Mr. BROWN proposed a new clause authorizing food and drugs authorities to enforce the provisions of the Bill relating

to advertisements and to the disclosure of composition of medicines and to institute proceedings against contraventions. Sir FRANCIS FREMANTLE said he understood inspectors of the Pharmaceutical Society would be able to carry out duties which otherwise would fall upon a common informer. The clause was added to the Bill.

Sir ERNEST GRAHAM-LITTLE moved and, after discussion withdrew, a new clause which proposed to prohibit the sale under a fancy proprietary name of any preparation having essentially the same composition as preparations listed in current editions of the *B.P.* or the *B.P.C.*

On the Report stage of the Bill on July 22, Mr. ERNEST BROWN moved a new clause providing that it should be the duty of the Pharmaceutical Society to take all reasonable steps to enforce the provisions of Clauses 3, 4, and 6 of the Bill, and for that purpose the Society might employ the inspectors appointed by them under Section 25 of the principal Act.

Mr. Brown moved a series of amendments to Clause 6 (Disclosure of composition of medicines). He said he had examined very thoroughly disclosure in everyday terms and had decided that wherever a well-known term existed it should be used. He had fallen back on disclosure in terms which would be readily understood by a doctor, chemist, or any other expert. The amendments would require disclosure in one of the following ways: (1) Where a medicine or a constituent was a poison in the Poisons List the name to be used was that required in connexion with the labelling of the poison. (2) Where a medicine or a constituent was not a poison but was described in the *British Pharmacopoeia* or the *British Pharmaceutical Codex*, the description at the head of the relevant monograph must be used. (3) Where it was neither a poison nor described in the *Codex*, the accepted scientific name or other name descriptive of its true nature must be used.

So far as quantitative disclosure was concerned, the amendments required the quantities of the named constituents to be disclosed either by giving the percentages in the medicine or stating the actual amounts. When a medicine was supplied in the form of pills and tablets, disclosure might be made in one of three ways: (1) the percentage of the constituent in the medicine ; (2) the quantity in each pill or tablet ; or (3) the quantity of the constituent in the whole article. The effect of the amendments together would be to require disclosure in English.

Sir FRANCIS FREMANTLE and Prof. A. V. HILL welcomed the amendments, which were agreed to.

Miss HORSBRUGH, replying to Sir Thomas Moore, reiterated that there was no desire to prevent herbalists carrying on their work. With regard to faith healers, there was nothing in the Bill to stop treatment of any sort or kind, nor to prevent anyone treating anyone else for any illness. Neither a herbalist nor anyone else was stopped from making any mixture under a proprietary name and selling it under a proprietary name so long as there was disclosure as provided in Clause 6.

The Report stage being concluded, the Bill was read the third time. On July 23 it was read a first time in the House of Lords.

Red Cross Brassard

In the House of Commons on July 15 Mr. LAW informed Sir George Jeffreys that the Geneva Convention, 1929, provided that to claim the protection afforded by the convention to military medical services, personnel of voluntary societies such as the British Red Cross Society must be subject to military law. The only members of the British Red Cross Society entitled to wear the Geneva Cross armlet were those incorporated with military medical units as determined by the Commander-in-Chief. Instructions were issued on this subject in March, 1940, and the position was subsequently made plain in correspondence with the British Red Cross Society in April of this year.

Women Doctors in the Services

Sir FRANCIS FREMANTLE asked on July 23 why women medical officers recruited to the Royal Air Force were not given the rank, status, and title accorded to male medical officers in the Service. Sir ARCHIBALD SINCLAIR said these women medical officers had the status of officers and the relative ranks pertaining to their duties and were addressed as medical officers. Sir FRANCIS said the title was not given. A woman medical officer was addressed as " Miss Smith, Medical Officer." Sir ARCHIBALD SINCLAIR said special designations applied in the case of women's Services such as the Women's Auxiliary Air Force and the nursing services.

On the same date Sir VICTOR WARRENDER told Sir Francis Fremantle that only one woman medical officer was employed in the Navy. She held the relative rank of surgeon lieutenant R.N.V.R., received the pay of that rank, and wore the distinguishing stripes of a surgeon lieutenant on her sleeve. If women doctors were supplied to look after the W.R.N.S. personnel that would mean duplicating the medical staff and would lead to inefficiency. Only 2½% of the W.R.N.S. expressed a wish to have women doctors.

Gas and Oxygen by Midwives

Replying on July 24 to Dr. Summerskill, Mr. BROWN said that according to returns made by local supervising authorities up to December 31, 1940, forty-nine of the 188 authorities concerned had made arrangements approved by the Central Midwives Board for instructing midwives in the administration of analgesics. Apparatus for administering analgesics was supplied by thirty-three authorities during 1940 as compared with twenty-one during 1939. Under special arrangements made by the Ministry of Health with the National Birthday Trust, forty-three machines had been supplied to emergency maternity homes in which the staffs were adequately trained in the administration of gas and oxygen.

Examination and Discharge of Unfit Soldiers. — Captain MARGESSON, replying to Mr. Rhys Davies on July 22, said that existing instructions already provided that, as soon as it became doubtful in the opinion of the medical officer in charge of the case whether a soldier in hospital was likely to become fit again for further military service, that soldier was brought before a medical board so that a decision might be given without delay. All soldiers had to be brought before a medical board before the end of five months' continuous absence from duty, or three months in the case of patients in mental hospitals.

Doctors and Appeal to the Courts.—Mr. GROVES on July 22 asked the Lord President of the Council whether, having regard to the right of dentists, pharmacists, and certain other professional persons to appeal to the courts against disciplinary decisions, appropriate steps would be taken to amend the law and give doctors a similar right. Sir JOHN ANDERSON replied in the negative. He said that he was not satisfied that there was any general desire in the medical profession for such legislation at the present time.

Medical Services in Invasion.—Mr. Ernest Brown states that, in case of invasion, all local medical and first-aid facilities will be made equally available for both military and civilian casualties in areas which become the scene of actual operations

Notes in Brief

A further Order under Defence Regulation 32 B is under consideration to include doctors resident in Great Britain who have obtained their degrees in Switzerland, Sweden, and other neutral countries.

Mr. Ernest Brown is in communication with Mr. Bevin about the rationing of materials used for occupational therapy in mental hospitals.

Mr. Bevin proposes to arrange that men who have been medically examined for the Armed Forces shall be informed that they should let the Ministry know if subsequently, while their calling-up is deferred, they think that their medical condition has deteriorated A further medical examination may be held in such cases.

Mr. Brown has decided that the Nursing Division of the Ministry of Health, the establishment of which was announced on April 3, shall deal with midwifery as well as nursing. The Division will be known as the Division of Nursing and Midwifery.

Asked when he proposed to publish a summary report covering the work of the Ministry of Health, Mr. Ernest Brown said on July 3 that the material was being collated as rapidly as more urgent work permits. There would be no avoidable delay in the publication of the Summary for the two years 1939-40 and 1940-1. Mr. Ernest Bevin was unable to state what action would be possible to ensure the issue in an abbreviated form of the report for 1940 of the Chief Inspector of Factories.

The number of nurses employed in factories has largely increased of late. Three special short courses, at which trained nurses can receive supplementary instruction in industrial nursing, have so far been arranged by the Ministry of Labour.

A draft report has been revised, for publication at an early date, of the medical part of the investigation by the Medical Research Council of silicosis among coal miners. Environmental studies form the subject of a second report which is being prepared.

No. 27

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended July 5.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1941					1940 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	201	15	51	2	5	178	14	32	1	5
Deaths		—	1				1	4		
Diphtheria	794	36	168	16	27	718	20	268	45	32
Deaths	25	1	5	—	1	23	—	4	1	3
Dysentery	61	4	34	—	—	34	1	41	—	—
Deaths			—	—	—			—	—	—
Encephalitis lethargica, acute	1	—	—	1	—	3	—	1		—
Deaths		—	—				—	1		
Enteric (typhoid and paratyphoid) fever	186	4	43	3	2	108	19	11	6	2
Deaths	3	—	—	1	—	—	—	—	—	1
Erysipelas		—	33	7	3		14	51	6	2
Deaths		—	—				—	—		
Infective enteritis or diarrhoea under 2 years										
Deaths	32	2	13	11	2	36	8	4	2	11
Measles	6,524	187	62	90	—	9,166	24	1,130	—	22
Deaths	5	1	1	2	—	5	—	9	—	—
Ophthalmia neonatorum	73	2	28	2	—	96	9	15	—	—
Deaths										
Pneumonia, influenzal*	680	23	4	—	5	441	20	3	—	8
Deaths (from influenza)	6	22	1	1	—	11	—	—	—	—
Pneumonia, primary			156	14				157	7	
Deaths		—		4	3		20		9	7
Polio-encephalitis, acute	2	—				1	—			
Deaths		—					—			
Poliomyelitis, acute	12	—	5	2	—	18	—	2	—	—
Deaths		—	—				—	—		
Puerperal fever	1	1	14	3	—	6	6	9	1	2
Deaths		—					—			
Puerperal pyrexia	158	9	18		1	130	14	6		—
Deaths										
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	787	23	112	42	17	1,128	34	150	46	53
Deaths	—	—	—	—	—	2	—	—	1	—
Small-pox	—	—	—		—	—	—	—		—
Deaths	—	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths			—	—	—			—	—	—
Whooping-cough	5,316	246	101	50	10	807	7	39	—	12
Deaths	28	3	4	1	—	4	—	2	—	1
Deaths (0–1 year)	273	21	66	33	11	288	38	47	17	25
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	3,898	460	584	168	99†	4,205	667	546	165	140
Annual death rate (per 1,000 persons living)			12.7	11.2	—			11.0	11.0	12.3
Live births	4,978	328	887	375	178†	6,088	929	840	394	256
Annual rate per 1,000 persons living			18.0	24.9	—			17.0	26.3	22.4
Stillbirths	208	18	41			214	23	38		
Rate per 1,000 total births (including stillborn)			44					43		

* Includes primary form in figures for England and Wales, London (administrative county), and Northern Ireland.

† Owing to evacuation schemes and other movements of population birth and death rates for Northern Ireland are no longer available.

EPIDEMIOLOGICAL NOTES

Infectious Diseases for the Week

Cerebrospinal and enteric fevers and pneumonia (primary and influenzal) increased in England and Wales during the week. In Scotland only enteric fever and diphtheria showed an increase, the former considerable, the latter very slight. In both countries acute poliomyelitis was more prevalent than last week, but the incidence remains low compared with last year and the year before.

Cerebrospinal Fever

During the six weeks ended July 5 notifications in England and Wales numbered 254, 244, 236, 211, 192, and 196 respectively. The disease is widespread, involving thirty-seven of the sixty-one administrative health areas in the country, but only in six were more than 10 cases notified during the week—namely: Lancaster 30 (Blackburn, Bolton, Bury, Crosby M.B., Droylsden, Fulwood, Kirkham, Litherland, and Warrington R.D. 1 each, Liverpool 4, Manchester 13, Salford 2, Clitheroe M.B. 2); Yorks, West Riding, 27 (Bradford 2, Doncaster 1, Rotherham 4, Sheffield 8, Keighley M.B. and Kiveton Park R.D. 2 each, and York C.B., Castleford, Cudworth, Normanton, Otley, Shipley U.D., Hemsworth R.D., and Rotherham R.D. 1 each); London 15 (Fulham 3, Lambeth and St. Pancras 2 each, Bethnal Green, Camberwell, Poplar, Shoreditch, Stepney, Wandsworth, Westminster, and Woolwich 1 each); Warwick 12 (Birmingham 8, Coventry 3, Meriden R.D. 1); Glamorgan 12 (Cardiff 4, Merthyr Tydfil 1, Swansea 2, Bridgend U.D., Gelligaer U.D., Llwchwr U.D., Neath R.D., and Pontardawe 1 each); Durham 11 (Gateshead 1, South Shields 2, Sunderland 4, Hetton, Ryton, Washington, Durham R.D. 1 each). In Scotland 300 cases were notified in the last six weeks, and in the first six months of the year 1,661, compared with 1,966 in the corresponding period of 1940. Eleven counties and eight burghs are at present involved, notably the counties of Ayr 6, Aberdeen 3, Fife 3, Lanark 3, and the burghs of Glasgow 15 and Edinburgh 4.

Enteric Fever

Of the total notified in England and Wales during the week, 46 more cases are of typhoid fever and the remainder of paratyphoid B fever. Nearly one-half of the total occurred in two areas, not more than 10 being notified in the other twenty-two areas for which notifications were received. The Birmingham and district outbreak of paratyphoid fever is declining, but cases continue to be notified in Stafford 47 (Stoke-on-Trent 40, Smethwick 1, Newcastle-under-Lyme M.B. 3, Tamworth M.B., Wednesbury M.B., Cheadle R.D. 1 each); Warwick 14 (Birmingham 10, Coventry 1, Solihull U.D. 2, Sutton Coldfield M.B. 1); Worcester 1 (in Kidderminster R.D.). Another area affected is Lancaster 35 (Blackpool 2, Bootle 7, Liverpool 21, Manchester 1, Southport 2, Morecambe and Heysham M.B. and Newton-le-Willows U.D. 1 each). In Scotland 6 cases of typhoid fever were reported (4 in Glasgow and 1 each in Ayr County and Arbroath burgh), and 37 cases of paratyphoid fever—namely: the counties of Angus 1, Fife 1, Lanark 5, Moray and Nairn 2, Roxburgh 2, and the burghs of Aberdeen 2, Dundee 17, Dunfermline 1, Glasgow 5, Edinburgh 1.

Diphtheria in Scotland

The unfavourable position in respect of diphtheria morbidity and mortality has led to a campaign which, it is hoped, will extend the benefits of immunization to children of pre-school age, even in rural districts. In two districts the medical officers of the clinic go round with a van to the remoter parts and have met with considerable success. During 1940 there were 15,711 cases and 676 deaths from diphtheria, compared with an average of approximately 10,000 cases and 410 deaths in the preceding four years; 50% of the deaths were in children between 1 and 5 years, and 83% between 1 and 10 years. So far 529,679 out of a child population of 1,124,500, or approximately 47% (65% in school children and 30% in pre-school children), have been immunized; lower figures were recorded in urban areas.

Dr. Arnulfo Aras, a well-known practitioner in Panama, who had formerly been Minister of Health as well as Ambassador to Italy, has been elected President of the Republic of Panama.

Medical News

Not least among the pleasures we have to forgo in wartime are the anniversaries of learned and scientific societies. But for the war there would have been fitting celebrations last week of the centenary of the Reading Pathological Society, which was founded on July 13, 1841, and is thus the oldest pathological society in the country. The meetings of the society during these 100 years have been held without a break at the Royal Berkshire Hospital, with which the society has always been closely associated. In 1900 the Reading Medico-Chirurgical Society, which dated from 1824, was merged in the Pathological Society, and its library transferred to the rapidly growing one at the Royal Berkshire Hospital. For the last fifty years each new session of the society has been opened with an oration by a prominent member of the profession, and the list of orators contains many distinguished names. The centenary was marked by a commemorative service in the chapel of the hospital, the presentation to the society of the considerable reference library which had hitherto been the property of the hospital, and a centenary oration, "One Hundred Years in Retrospect," by Dr. G. O. Lambert, senior honorary physician to that institution.

Lieutenant-Colonel Henry Guest, M.P., presiding at the annual meeting of the London Chest Hospital, Victoria Park, E., said that despite very severe damage in recent air raids such good progress had been made in first-aid repairs that the hospital had now been reopened for in-patients and all departments had resumed working. A start had been made with the building of a new pathological department to replace the one that was completely destroyed, burying records and specimens representing ninety years of research on chest affections.

It is reported in the *Journal of the American Medical Association* that a blood donor centre has been organized in the Augusta-Victoria Hospital in Berlin.

The Trustees of the Dr. Jessie Macgregor Prize in Medical Science announce the award of the prize for the present triennial period to Miss Agnes Rose Macgregor, M.D., F.R.C.P.Ed., for her work on pneumonia in the newborn. The prize is open to medical women who are graduates in medicine of the University of Edinburgh or who have taken the triple qualification of the Scottish Medical Corporations. It is awarded to the applicant who presents the best record of original work in the science of medicine during the past three years, and is of the value of £75.

A certificate presented to Parliament by the Prime Minister enables Prof. A. V. Hill, Sc.D., F.R.S., who has become an Associate Member of the Ordnance Board, to retain his seat in the House of Commons as one of the Members for Cambridge University.

The names of Mr. Charles Alfred Keogh, F.R.C.S., surgeon, London, and Dr. Alexander Hendry MacKie, medical practitioner, Birmingham, have been brought to notice for brave conduct in civil defence.

Dr. Kenneth R. Hay and Mr. H. S. Souttar have been elected Managers and Dr. Russell J. Reynolds a Visitor of the Royal Institution.

Sir John Boyd Orr, M.D., F.R.S., Director of the Rowett Research Institute, has been re-elected president of the Aberdeen branch of the Children's Nutrition Council.

A Pan-American League against Cancer has been founded in New York under the presidency of Professor Angel H. Roffo, director of the Institute for Experimental Medicine in Buenos Aires.

At Baltimore the Public Health Service maintains a tumour clinic which serves as a demonstration of the life-saving possibilities of adequate cancer treatment. In the first eight months of its existence 226 patients were treated.

Switzerland will celebrate the 400th anniversary of the death of Paracelsus at Einsiedeln from September 27 to 29.

Professorships of industrial hygiene have been established at Turin, Sienna, and Padua, so that with those at Milan and Naples Italy now possesses five such chairs.

Letters, Notes, and Answers

All communications in regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, W.C.1.

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QUERIES AND ANSWERS

Income Tax

Change from Employment to General Practice

"J. G. M." was employed as an assistant up to the end of April, 1941, earned £28 as a locumtenent in May, and has since started in general practice. He is still being asked to pay tax on his employment earnings.

*** The tax payable on the salary as assistant for the year to April 5, 1941, would normally be deducted in equal monthly amounts over the period November 1, 1940, to October 31, 1941. Presumably when "J. G. M." left his employment at the end of April there would be some tax not then due for deduction, and therefore not paid. He is liable to account directly to the Revenue for that balance of his liability for 1940-1. In addition, of course, he will ultimately have to account for the liability (if any) on his earnings of April, 1941, as part of his income for 1941-2.

Appointment: Car Allowance

"F." holds a full-time appointment as M.O.H. and receives a car allowance of £100. This amount is inadequate in war conditions, but the inspector of taxes refuses to make a deduction for the excess expenditure.

*** The rule applicable to Schedule E is strict—expenses to be allowable must be "incurred wholly, exclusively, and necessarily in the performance of the duties of the office." The inspector presumably takes his stand on the assumption that whatever amount "F." in fact expends, the appointing authority have made an allowance on the basis that £100 covers *necessary* expenditure, and we think that in the absence of other evidence that is likely to be the view taken on appeal to the local commissioners. Possibly "F." could obtain a statement from his authority that while they are unable to increase the allowance they no longer regard it as adequate to cover necessary expenditure. That would be very helpful evidence in support of his claims.

Reduction in Practice Income

"HARD HIT" has a partnership in a practice which has suffered severely owing to the war, with the result that the previous year's basis works harshly.

*** If—as is apparently the case—"Hard Hit's" earned income calculated on the basis of the actual year is not more than four-fifths of the earned income as assessed he can claim to have his liability adjusted to the actual year's basis. An application should be made to the Inspector of Taxes accordingly, and should be made by each individual partner and not by the firm as such. As regards the current financial year, tax will not be payable until January, 1942, and if the necessary accounts are not then available no doubt some arrangement can be made for the acceptance of a payment on account.

Dominion Income Tax Relief

"A. T." has income from a Dominion on which £10 10s. income tax is paid there. He has been refunded £7 by the British Government, but this £7 is being taxed as income.

*** Prior to the introduction of this relief the tax paid in the Dominion was regarded as deductible in calculating the liability to British income tax—i.e., "A. T." would have been assessed on, say, £100−£10=£90 in full. The present position is that relief can be claimed in respect of the Dominion tax up to a maximum determined by half the "appropriate rate" of British tax payable by the claimant. In so far as this relief reduces the amount suffered by payment of Dominion tax, that tax ceases to be

deductible in calculating the amount of the income for assessment to British tax. The relief as suggested above does not extend in many cases to the whole of the Dominion tax; if it did there would be no inducement for reciprocal action on the part of the Dominion concerned.

Reduction in Civil Earnings

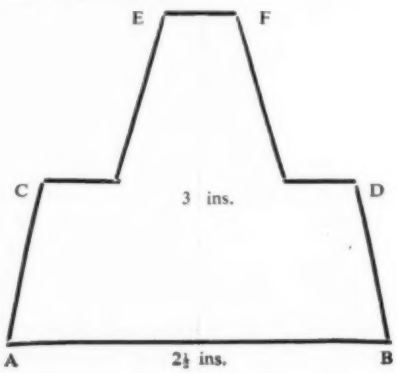
"MILES" is serving in the Forces, his practice being run by a locumtenent. Can he claim to deduct the whole of such expenses as maid's wages and upkeep, gas, light, and telephone?

*** In the circumstances it seems reasonable that a higher proportion than formerly should be claimed and allowed, but so long as a part of the premises is not being used for professional purposes—the rooms occupied by the locumtenent being regarded, however, as used professionally—"Miles" will be unable to enforce a claim to allowance of the *whole* of such costs. If the actual total income of "Miles" for 1940-1 is not more than four-fifths of his earned income for that year he can claim to have the assessments adjusted to the actual basis.

LETTERS, NOTES, ETC.

Treatment of Cracked Finger-tips

Dr. M. R. SONI (Manchester) writes: Cracked finger-tips are very common in winter. Persons with soft skins who have not done any manual work and who are new to war work suffer especially from this painful condition. As a preventive and curative measure elastoplast should be applied in the following manner after cleansing the hand thoroughly with grease-solvent soap and paring the edges of the crack with a safety-razor blade. Cut the plaster in the manner illustrated below:



Place the tip of the finger (beyond the distal joint) along the side AB in its centre. Bring down EF over the finger-tip and the nail and stick it to the dorsal surface. Pull on the sides AC and BD and press their adhesive surfaces together in the middle line. Cut off all redundant plaster and mould the dressing to the form of a thimble. In this manner elastoplast makes a neat little dressing for the finger-tip which need not be disturbed for a few days. I have known patients to do work of a delicate nature wearing "thimbles" on all the finger-tips. The dressings stand wear and tear, and are to some extent waterproof. If the surface of the skin is broken a little plain zinc ointment should be applied to the wound on a small piece of lint before covering it up with plaster. As a corrective measure a little "HEB" (protective) should be rubbed into the hands night and morning. This preparation is manufactured by J. Halden and Co., Ltd., of 37, Brazenose Street, Manchester, according to the formula of Dr. P. B. Mumford (see *British Medical Journal*, February 11, 1939, p. 266.)

Attending a Colleague

"SCOTIA" writes: In a recent issue of the *Journal* a suggestion was made as to how medical practitioners could repay specialists for their attendance on them. I would suggest that every doctor voluntarily should pay £1 1s. annual subscription for himself and an additional £1 1s. for his wife and children into a general fund, which would amount to many thousands a year. From this specialists should be paid a standard but not reduced amount, and this would make it easier for the general practitioner to approach the already too willing specialists. Each hospital could provide a room for the use of the patient; the hospital would be paid the usual private room fees from the fund. The medical profession as a whole are not often patients and not for longer than is necessary, so that eventually from the same subscription a sickness insurance might be possible. This insurance should be entirely in the hands of the profession to avoid unnecessary expenses.

Minerals and Vitamins in a "Health Dinner"

In a bulletin issued by Vitamins Ltd. (which can be obtained on application to the firm at 26, Upper Mall, London, W.6) the following food values are given for a modified "Oslo breakfast" recently given to a group of London school children as a "health dinner."

	Vit. A Units	Vit. B_1 Units	Vit. C Units	Vit. D Units	Available Iron mg.	Calcium mg.
Salad: lettuce 1 oz. ..	934	6	62	—	0·10	7·0
tomato 1 oz...	844	7	138	—	0·03	1·0
cucumber 1 oz.	—	5	40	—	0·09	6·3
carrot 1 oz. ..	534	5	11	—	0·16	15·0
Cheese 1½ oz. ..	937	2	—	5	0·24	345·0
Butter ½ oz.	738	—	—	10	—	3·0
Milk ½ pint	812	50	—	7	0·30	440·0
Wholemeal bread 3 oz.	170	93	—	—	1·74	30·0
Fresh fruit 3 oz.(apprx.)	84	23	750	—	0·30	19·0
Totals ..	5053	191	1001	22	2·96	866·3
Daily requirement for health	6000	600	1500	400	10–12	1000

Roughage in Food

Dr. JOSIAH OLDFIELD writes: I think the medical profession should set their faces against the word "roughage," which has been introduced of late years by writers on dietary. It gives a wholly unscientific view of the processes of digestion, assimilation, and defaecation. "Roughage" gives the idea that the alimentary canal works by a process of irritation, and anyone who uses the word thinks of it as something which scrapes along. This fallacy has made the fortunes of patent medicine vendors, because owing to the conditions of modern life constipation is one of the commonest ailments of humanity. The majority of patented medicines, and even of prescriptions given by the medical profession, are based upon the use of either vegetable or mineral irritants. Study of digestion teaches that this is an entirely fallacious method of looking at the physiological processes which accompany the intake of food and the excretion of waste matters. In a cow (which is one of the best illustrations I know of an animal that never suffers from constipation), the contents of the second stomach after the chewing of the cud could never, by any stretch of language, be called "roughage," and yet those who have ever kept cows would admit that there is no animal they know in which the digestion is so easy and certain. The alimentary canal works on the harmonious relation between the muscular structure of the intestinal walls and the contents of the intestine. This relation is not one of irritation but entirely the reverse. The human animal should always be in a state where the contents of the alimentary canal afford the soothing stimulus and the necessary mass for the musculature of the walls to function upon. We find as an experience that when men live upon "the kindly fruits of the earth" constipation is unknown. It is not the coarse corn and the modern foods made of bran which are the harmonious foods, but the admixture of vegetables of the garden, fruits of the orchard, grains of the harvest field, and oils and fats of the nut tribes which will always provide a suitable bulk, a suitable stimulant, and a suitable mass for muscular action. To these foods may be added products of the dairy, such as milk and cheese, and eggs, though these are all comparatively constipating; but no constipation can ever persist where the food consists largely of the products of the earth.

Skin and Mind

Dr. E. SAKOSCHANSKY (Southampton) writes: I have read your annotation on skin and mind (July 12, p. 55). In my opinion there is no need for such apologetics as "apt to begin with confusion and end with incredulity" or "avoid the role of obstructionist," etc. After all, the brain is derived from the skin: it is no more than an invagination of an especially sensitive part of the skin. Both the brain and the skin are rich in cholesterol; therefore both probably react in a similar way to certain metabolites and ions. Hence it follows that the "frequent association of certain allergic phenomena with a particular type of personality" may be due to a similar make-up in the skin and in the brain.

Accommodation for Doctor's Child

Dr. X. Y., who practises in a small country town in the Cotswolds, offers accommodation to a doctor's child, preferably a girl between 3 and 5 years of age, from a "blitzed" area. Dr. X. Y. has two children, a girl of 4 and a boy of 2. Accommodation is offered, in return for actual expenses only, either for the summer or for the duration of the war. Letters addressed to Dr. X. Y., c/o the Editor, will be forwarded.